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A TEXT-BOOK

OF

PATHOLOGY

FOR PRACTITIONERS AND STUDENTS

By

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TO

George H. Horn, M. D.
William Stevens, A. M.
Charles Walter, M. D.
William Osler, M. D.

FRIENDS WHOSE INFLUENCE DURING BOYHOOD, YOUTH, AND
EARLY MANHOOD HELPED TO MAKE ME, AND
SO TO MAKE MY BOOK

PREFACE.

THE author, having taught Pathology and Bacteriology for thirteen years, endeavors in the following pages to present in a succinct, intelligible, and readable manner the facts that every student should know before he advances from the elementary to the practical branches of medicine. The work has been written particularly for students working for the degree of Doctor of Medicine, who need to acquire the principles of pathology rather than to busy themselves with the evolution of the subject or to enter into the consideration of its controversial points. Well-known facts are, therefore, presented as such, while others are frequently dismissed after brief mention with the frank statement that the matter is not yet understood.

Over-voluminousness was the greatest evil that had to be overcome in the writing, and what could be consistently omitted was a far greater problem than what should be introduced. The natural impression of the author was that nothing should be omitted; but the size of the manuscript became, and after careful condensation remained, so large, that something had to be done lest its usefulness be destroyed. A kind of compromise was eventually effected by the use of two sizes of type, the more important matter being printed in the standard type and the less important in smaller type.

The standard works have been freely consulted and drawn upon, though the names of the authors and the references to their writings have been for the most part omitted, as the work was not designed to be in any sense encyclopedic. The illustrations have been selected for the purpose of assisting the reader to comprehend the text. Many of them are original, but the author has to thank the writers and the publishers of a number of well-known books for their courtesy in permitting him to use illustrations from their works. The borrowed illustrations have been duly credited to the authors from whose writings they have been selected.

PHILADELPHIA, June, 1904.

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A TEXT-BOOK

OF

PATHOLOGY

McFARLAND

PART I.—GENERAL PATHOLOGY.

INTRODUCTION.

Scope and Terms of Pathology.—"Pathology is that subdivision of biology that has for its object the study of life in its abnormal relations." It is the study of diseased conditions, and aims at the discovery of the changes of organization and function that result from all abnormal conditions.

Health exists when the normally constructed body properly performs its functions. Disease is any variation from this normal standard, and may be described as any condition in which the organism finds itself in abnormal relationship with its environment. *Disease* is, therefore, a general term signifying any variation from the normal condition. *A disease* is a condition characterized by the occurrence of definite phenomena and constituting a recognized type of abnormality. Thus, fever is a diseased state or condition found in many different diseases. Typhoid fever, a febrile affection with definite symptomatology, is a disease.

In the scope of pathology are included the source, progress, changes, and terminations of disease. A knowledge of pathology forms the only rational foundation upon which the art of medicine can rest, as it is through its teachings alone that symptoms can be understood and treatment properly applied. The chief contrast between the medical art of the ancients and of the semi-civilized nations and modern medical science is the ignorance of pathology on the one hand, and an increasing knowledge of it on the other. Until our knowledge of biology in its normal and abnormal relations is perfected, medicine cannot become an exact science.

It is customary to divide the subject into *General Pathology*, that deals with disease processes common to the whole organism, as fever, cachexia, degeneration, etc., and *Special Pathology*, in which the diseased conditions of the special organs are considered.

Morbid Anatomy, Morbid Histology, and Morbid Physiology, or, as they are frequently called, Pathologic Anatomy, Histology, and Physiology, contemplate respectively the gross and minute structural and functional changes.

Nosology, or the Classification of Disease.—Diseases are variously classified according to the standpoint from which they are viewed. Thus, they are spoken of as *hereditary*, if actually derived from one or both parents; *congenital*, if appearing at birth, but not necessarily referable to the parents; and *acquired*, if appearing subsequent to birth.

According to their time of occurrence, diseases are also described as *infantile* in babyhood, and *senile* in old age.

According to their origin, certain diseases are described as *zymotic*, *infectious*, or *specific*, when they depend upon living entities, such as bacteria, protozoa, insects, worms, etc. Some of these diseases that can be communicated by touch are called *contagious*. *Miasmatic* diseases were formerly supposed to depend upon certain deleterious influences exerted by the soil; at present no true miasmatic disease is known.

According to their manner of occurrence, diseases are described as *sporadic*, when isolated cases occur at irregular intervals; *epidemic*, when

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large numbers occur at the same time; *endemic*, when a disease is continuously present in a community; and *pandemic*, when everywhere, in all countries, nearly everybody is more or less influenced by a disease.

Toxic diseases depend for their origin upon the presence of poisonous substances, either derived from external sources or manufactured in the body, either by parasites or by its own metabolic processes abnormally carried on.

According to their lesions, diseases are described as *organic* and *functional*: *organic* diseases being characterized by definite lesions of the organs and tissues; *functional* diseases having no discoverable lesions, and manifesting themselves only by disturbed physiologic action. Organic diseases are anatomic, functional diseases physiologic in character.

The distribution of disease makes it either *local* or *general*. *Constitutional* diseases are general diseases whose hold upon the organism is such as to affect its very constitution or functional organization.

The duration of disease is variable, so that all morbid processes can be classified as acute or chronic.

Acute diseases are of abrupt onset, active symptomatology, and short duration. *Chronic* diseases, on the other hand, are of insidious onset, mild symptomatology, protracted duration, and progressive lesions. *Subacute* affections are neither acute nor chronic, but often begin as acute diseases, running protracted courses and healing slowly.

Ephemeral or *fugacious* diseases are acute processes of exceedingly short duration. *Continued* fever is of protracted duration.

With advancing knowledge the number of diseases for which it is impossible to find an adequate cause has greatly diminished, but, unfortunately, the term *idiopathic* is still employed to describe them. Diseases with recognizable causes are known as *symptomic*.

According to their occurrence, diseases are described as *primary*, *secondary*, *tertiary*, and *recurrent*.

A *primary* disease is the first occurrence or expression of disease. A *secondary* disease depends upon some primary disease. *Tertiary* disease is seen in syphilis, and refers to the third set of symptoms of that affection.

Diseases also vary in their tendencies. Some are *benign*—that is, tend to recover without materially injuring the patient; while others are *malignant*, and tend toward his final destruction. A few diseases are called *fulminant*, because of the extreme rapidity and severity of their symptoms.

Recurrent diseases are characterized by a tendency to recur or come back, as in the case of malignant tumors. Recurrent fevers are called *relapsing*.

Intercurrent affections develop during the course of some other disease, as when a person suffering from tuberculosis of the lungs is attacked by pneumonia and dies of it before the tuberculosis had become sufficiently far advanced to endanger life. The pneumonia is then described as intercurrent.

The structural changes wrought by disease are known as *lesions*. They may be *initial* or *primary*, *secondary*, or *tertiary*.

Nosogeny, or the Development and Progress of Disease.—It is best considered in relation to certain of the specific febrile affections, in describing which all of the employed terms are used. These affections result from the presence of parasitic bacteria which enter the body, producing what is called the *infection*. For a time subsequently they increase in numbers and elaborate metabolic products that shall be the cause of subsequent changes. This period is, therefore, a latent one, during which development is going on, and is known as the *period of incubation*. During it vague symptoms are not infrequent, but are indefinite and not very severe; they are called *prodromes*. The recognized disease is not infrequently ushered in by definite symptoms that may be slow and insidious, or abrupt or explosive, and constitute what is known as the *invasion* or *onset*. The disease now pursues a course that for some time may be without much variation, constituting what might be termed the period of active disease, and is called the *acme* or *fastigium*. Subsequently comes a period of *decline*, that marks the beginning of recovery, followed by a more or less rapid gain of strength and return to the normal state during *convalescence*.

The time of *infection* may pass unnoticed ; or, on the other hand, may be referred to some particular moment, as when some wound, accidentally or intentionally inflicted, was the point of entrance of the disease-producing germs.

The period of *incubation* is very variable, depending upon the ability of the micro-organism to bring about its effects. Septic infections may develop in a few hours. Tetanus, or lockjaw, has an incubation period of from three to ten days ; hydrophobia, one that is said to vary from weeks to months.

The onset or *invasion* varies with each disease. Pneumonia has a sudden invasion, characterized by a chill, followed by cough, dyspnea, etc. In typhoid fever there is a progressive slow increase of temperature, lasting over a number of days, the temperature each evening being about a degree higher than in the morning. The exanthematous fevers of childhood are frequently ushered in by reflex symptoms, such as vomiting, headache, and convulsions.

The *fastigium* also varies, some diseases scarcely developing before their decline begins ; others, as typhoid fever, continuing for one or two weeks. When the fastigium is without marked alterations, it is said to be *continuous*, as in typhoid fever. In the malarial fevers extraordinary fluctuations are observed, the high fever being interrupted by *intermissions*, during which the temperature returns to the normal ; or *remissions*, during which it falls below its customary altitude, but not to the normal. Sometimes the course of a disease is marked by occasional *paroxysms* or *exacerbations*, during which all the symptoms may become greatly exaggerated or renewed, or entirely new symptoms develop, as in the course of tetanus, with the tonic spasm of trismus for a constant symptom, and clonic spasms with opisthotonos at intervals.

The period of decline is not without interest, for, while the greater number of diseases end by a gradual amelioration of all the symptoms, or *lysis*, a few are characterized by a sudden disappearance of the serious symptoms and immediate improvement, this being known as *crisis*.

Convalescence is brief or protracted according to the extent of the damage to be repaired. Sometimes during convalescence the symptoms all reappear, and a *relapse* or repetition of the disease, usually less severe than the original affection, makes its appearance. There may be several relapses, and patients who have successfully passed through the disease may die in the relapse. Any exacerbation of disease, as well as a relapse, may be described as a *recrudescence*.

The *termination* of disease may be in a more or less complete return to health, or *recovery*, as in most of the acute affections, or in *death*. Incomplete recovery also sometimes occurs, producing a chronic or indefinite continuance of the morbid process. After recovery from a disease, other diseased conditions depending upon conditions set up by the original process may appear. These are *secondary diseases* or *sequelæ*. Thus, after diphtheria it is common for paralysis of certain groups of muscles to occur from toxic injury to the nerves. In diphtheria and typhoid fever remote abscesses sometimes result from the entrance of pyogenic bacteria into the blood from the lesions of the disease. After pleurisy and pericarditis fibrous adhesions may deform the chest and embarrass the circulatory and respiratory functions. Peritoneal adhesions following peritonitis may lead to obstruction of the intestines and to death. The sequelæ of disease are, therefore, important, serious, and sometimes themselves fatal.

CHAPTER I.

THE ETIOLOGY OF DISEASE.

To define disease as an inharmonious relation of the individual to his environment is sufficient to suggest what multitudinous factors have to be considered under the head of etiology. The individual may be congenitally deficient in parts and unable properly to perform his functions; or he may inherit from his parents certain vices that pervert his nutrition and cause fatal weakness; or he may accidentally lose important members and miss their absent functions; or he may become the host of parasites which absorb his nourishment, poison him with their products, or transform his tissues into useless perversions; or he may become intoxicated through extrinsic poisons taken in the air, food, or water; or his metabolism may become defective and he may succumb to poisons generated within his own body. Add to these the rigors of climate, the fury of the elements, the feebleness of youth and the miseries of old age, and it will be seen that the "devils by which we may be possessed can truly be called legion."

The factors involved in the etiology of disease may be divided into *intrinsic* and *extrinsic*.

I. INTRINSIC FACTORS IN THE ETIOLOGY OF DISEASE.

Heredity.—This term is much misused in medicine, being applied to many prenatal conditions that have nothing to do with it in the true biologic sense.

In biology the term heredity is used to describe conditions transferred from parent to offspring through peculiarities of the germ plasm. It does not refer to accidental conditions of prenatal life by which the health or perfection of the offspring is affected.

It has not been determined through what means the hereditary transmission of peculiarities—especially acquired peculiarities—takes place. All theories thus far suggested fail to explain the phenomena.

Biologists differ as to whether acquired characteristics can be transmitted to offspring or not. If not, then there cannot be such a thing as a hereditary disease or deformity.

Lamarck and Darwin believed firmly in inheritance and in the transmission of acquired characteristics, and Darwin made it the basis of his theory of evolution. Weissmann, and perhaps a majority of the biologists of the present day, doubt or disbelieve its possibility. It seems certain that experimental characteristics are not transmitted—*i. e.*, mutilations such as result from circumcision, amputations, scolisectomy, etc., are not transmitted, but it appears certain that spontaneously acquired variations from the normal may be transmitted.

Adami has suggested that heredity may be explained upon the assumption that the *idioplasm*, or that part of the protoplasm possessing vital properties, is composed of a mass of molecules which form a central ring, to which side rings may be attached or from which they may be detached without alteration of the central primitive ring. Environment causes the central ring to have attached certain side-chain combinations, and in this way the modifications of tissue cells are consummated. In the same manner environmental conditions lead to further modifications in the form of new lateral-chain combinations. Those lateral chains which are last developed are the least stable and the most readily lost, while those which have been attached for a long period of time are not readily loosened. Thus it is that recent changes in structure or alterations of environment produce with the general idioplasm combinations too weak to be transmitted, while lateral chains which have been active for generations tend to persist.

In sexual conjugation, idioplasms with different lateral-chain combinations and affinities unite, and there results an idioplasm not possessing the identical properties of either parent, but emendated in character and constitution toward the constitution of either one or the other, according to the preponderance in number or chemical activity of the molecules entering into combination. This hypothesis explains parasyphilitic lesions, for example, as a result of the transmission to the child of an idioplasm that had acquired certain abnormal chemical combinations as a result of parental infection. Or the transmission may be by intoxication, the intoxication being represented by a combination of toxiferous molecules with the idioplasm that is transmitted to the offspring.

Consanguinity and **inbreeding** are dangerous from their tendency to accentuate family weaknesses, this danger being in proportion to the deviation from the normal of those concerned.

False heredity or **apparent heredity**, commonly mistaken for heredity, consists in the modification of the embryo by conditions occurring during prenatal life. Thus, certain infectious diseases, such as small-pox and syphilis, may be transferred from mother to fetus through the placental circulation and cause a disease acquired from the parent. It seems, however, that in the case of syphilis the cause of the disease can be contained in the germ cells themselves and grow concomitantly with the embryo, thus causing infection at the very moment of impregnation. Here again, however, we have to do with an extraneous infectious element, and though the cause of the disease is contained in the germ plasm and the disease is handed down from parent to offspring, it is not hereditary in the true biologic sense, but is an example of apparent heredity.

The hereditary conditions thus far considered refer to immediate peculiarities; thus, the parent having a peculiarly situated lock of white hair transmits the peculiarity to the child; or the parent has six fingers or toes and the child has the same; or some other marked peculiarity of the parent is observed in the child. Hereditary conditions, especially in connection with certain diseases, are, however, more remote; thus, in hemophilia or "bleeder's disease" we find a certain mode of transmission, the males suffering from the disease may not transmit it to their immediate offspring, though their daughters are very apt to transmit it to their sons, thus skipping a generation.

A peculiar reversal to primitive structural types is seen in what is known as *atavism*, in which the traits of remote ancestors may make their appearance. Among these may be mentioned flat-foot, prognathism, receding forehead, projecting and massive ears, all characteristics of the lower races and of the simian family. Individuals possessing well-marked atavistic structural defects are commonly observed to be mentally and morally deficient as well.

Hereditary tendencies or predispositions, such as occur in the offspring of tuberculous, cancerous, and neurasthenic subjects, may depend upon transmitted physiologic peculiarities or may be nothing more than the result of lack of vigor of the germ plasm, whose development results in a feeble individual.

Congenital diseases have nothing whatever to do with heredity, but depend upon accidents of prenatal life.

Age.—Age has a distinct influence upon the occurrence of disease. In general it may be said that the extremes of life show the greatest predisposition to disease. Certain diseases, usually mild infections, are characterized as "children's diseases," though they may occasionally attack adults, and may be fatal both to children and adults. Among these are mumps, measles, chicken-pox, rötheln, scarlatina, and pertussis. Children are markedly predisposed to gastro-intestinal disturbances in consequence of the delicacy of the digestive organs. They are protected from many of the diseases of adults that depend upon exposure to the elements or upon free association with other persons.

At the time of adolescence a number of physical and mental disturbances may occur. With early adult life women begin to experience the dangers and consequences of childbirth, and men are apt to show marked increase in venereal affections. About middle life the results of youthful indiscretions may show their effects, and the cares and worriments of social life begin to tell upon the nervous system. Beyond middle life the tendency to carcinoma increases markedly and fibrosis of the organs makes its appearance. With old age comes the brittleness and inelasticity of the blood vessels, predisposing to apoplexy, uremia, etc.

Sex.—Sex exerts a very marked determining effect upon disease, both because of the structural and physiologic differences between the male and female, and because of the peculiar social conditions affecting each. Women, of course, suffer from affections incident to childbirth, and on this account are predisposed to special ills, but notwithstanding it, they usually live protected and moderate lives; while men are abroad, exposed to the elements and tempted to excesses of all kinds.

Up to about the fifteenth year—*i. e.*, until after puberty, there is no considerable difference as to morbidity and mortality between the sexes. With increasing years, however, males show a preponderance in regard to alcoholism and other forms of intoxication, typhoid fever, rheumatism, urinary and venereal diseases, cirrhosis of the liver, kidneys, and nervous system; while females suffer more markedly from anemia, cancer, peritonitis, and intrapelvic tumors having their origin in the sexual organs.

Hemophilia is essentially a disease of men; osteomalacia a disease of women.

Race.—While natural immunity to different diseases is characteristic of different animals, there are but few striking illustrations of it among the different races of men. It is said that the Japanese are immune against scarlatina, the Chinese against cholera, and the negro against yellow fever. These forms of immunity are, however, possibly less positive than is usually claimed. The apparent exceptional severity of measles among adults in the Fiji Islands and among other savage peoples may be but the natural course of the disease among those not protected by infection in youth. Jews are said to be predisposed to diabetes and resistant to tuberculosis.

Many of the racial susceptibilities may be no more than the result of abnormal environment and habit; as, for example, the frequency of tuberculosis among Indians, Esquimaux, and other savage peoples introduced into civilized society. Some may also depend upon diet, the cereal-eating Oriental races having less resisting power than the meat-eating peoples of the Occident.

II. EXTRINSIC FACTORS OF DISEASE.

Physical Agencies.—The lesions caused by physical agencies are said to be *traumatic*, and vary with the nature of the force.

Mechanical forces effect changes in the body according to the extent, severity, rapidity, and duration of their action. We may consider the action of such forces under the separate headings of Pressure, Contusion, Laceration, Incision, Perforation, and Concussion.

Pressure.—Continued pressure is followed by atrophy because of the resulting malnutrition. Intermittent pressure causes atrophy, deformity, or hyperplasia according to the associated conditions. Wearing heavy leather aprons tied about the body by cords is a frequent cause of atrophy of the subcutaneous tissue and adipose tissue beneath the cord. The pressure of a tightly fitting corset upon the costal cartilages causes them to turn in, thus lessening the capacity of the upper part of the abdomen. This deformity of the chest wall brings the edge of the costal cartilages in contact with the liver, which is pressed upon and atrophies, sometimes to the extent of being almost cut in half, the parts being connected by the fibrous tissue of the organ only.

The pressure of an ill-fitting shoe upon the toes may cause hyperemia, succeeded by an epithelial overgrowth and the formation of a corn. The hands of oarsmen become callous from epidermal thickenings, and the finger-tips of violin players show marked horny protections.

When solid bodies enter the body and remain there, whether they are as small as the particles of coal dust in anthracosis, or as large as musket balls, they keep up a persistent pressure upon the surrounding tissues that is succeeded by connective-tissue proliferation.

The weight of the body itself pressing upon its skeleton is the cause of bony deformities in such diseases as osteomalacia and rickets.

Contusion results from sudden forcible contact with blunt objects. It is a frequent form of injury, and usually causes damage of the contused tissues, depending upon the force and character of the resistance. The energy of any force is equal to one-half of the product of its mass into the square of its velocity. The velocity is, therefore, much more important than the size. Contusions usually result in "bruising" the tissues, which appear upon the surface to have a dark-purple color from ecchymosis of blood from injured capillaries. Swelling is always present. Bones contused are frequently fractured and not infrequently comminuted.

The effects of contusion are sometimes transmitted and focus upon distant points, as in the fracture of the skull opposite the point struck, in what is described as "*contrecoup*." The effects of contusion sometimes appear in the internal organs without lesions of the skin, for similar reasons.

Laceration is mechanical injury accompanied with breaches in the continuity of the tissue affected. It may result from the same forces producing contusions, but usually depends upon contact with sharper objects or upon greater velocity of the damaging force.

Laceration cannot occur without rupture of blood vessels and other important structures. As the force both crushes and tears the tissues the hemorrhage is usually not great, though the damage to the soft parts is very considerable.

Incision results from contact with keen and sharp objects. It results in cleanly opened wounds, in which the blood vessels, being freely opened, bleed actively. The tissues incised are completely severed. Such wounds heal most kindly because the injury scarcely extends beyond the surfaces of the wound.

Perforation results from pointed objects and from small objects with great velocity, such as bullets, arrows, etc. The damage will depend entirely upon the nature and velocity of the object. A clean dagger wound may not differ materially from an incised wound. An arrow with a crudely chipped flint head gives a combined contusion, laceration, and perforation that heals less readily.

In the case of gunshot wounds the chief difference will depend upon the velocity of the projectile. The higher the velocity of the projectile the less it influences the tissues with which it comes in contact; the lower the velocity the more it damages them. The modern rifle bullet of small caliber is far less destructive to the tissues than the old musket ball, chiefly because of the difference in velocity. A spent ball does much more harm than one moving rapidly. It is because the projectile has its velocity diminished by the resistance of the tissues that the wound of exit is more serious than that of entry.

Concussion is a violent agitation of the body, resulting chiefly from severe jars. It may depend upon conditions already described, or without them, as in explosions with the terrible rending effect of the enormous pressure of the liberated gases. Jars of the central nervous system may produce *commotio cerebri*.

Traumatic injuries of all kinds, but chiefly those associated with breach of continuity of the skin, predispose to infection according to the extent of the devitalization of tissue. The greater the devitalization the greater the loss of resistance to bacterial invasion.

Temperature.—The extremes of temperature are incompatible with life.

Heat can be compensated for to a limited extent by the cutaneous perspiration, the evaporation of which keeps the skin surface moist. As soon as the temperature reaches 55° C. this compensation becomes insufficient and death follows, preceded by anxiety, headache, accelerated cardiac and respiratory activity, and convulsions or asthenia.

A brief exposure to very high temperatures (200° C.) may be safely made in a perfectly dry atmosphere.

Burns result from the local effects of excessive heat. Four classes of burns are described, and sufficiently explain what takes place: 1, Hyperemia of the exposed surface; 2, extravasation of serum and colliquation of certain cells, leading to vesication; 3, coagulation of the cytoplasm of the cells, resulting in necrosis and extending more deeply into the tissues; 4, more or less complete oxidation or incineration of the tissues, extending to and even affecting the bones.

Following extensive superficial burns, the withdrawal of large quantities of serum from the blood is followed by anhydremia with hemolysis and a tendency to thrombosis. The excretory organs are injured by the altered quality of the blood and the kidneys may cease to functionate properly. There is diminished oxidation of the tissues, with a tendency to fatty degeneration.

In some cases of extensive superficial burns, death has resulted subsequently from a perforating ulcer of the duodenum, the mechanism of whose formation is not clear, but may depend upon thrombosis of some of the small vessels and corrosion by the entering gastric juice.

Cold.—General reduction of temperature is much more difficult to compensate for than general increase. Unless the body be protected by clothing, so as to prevent the radiation of heat, its combustion is insufficient to meet the requirements of even ordinarily severe climates. When exposed to low temperature the cells of the body fall into a condition of rigidity that gradually ascends to the nervous system, whose cells becoming rigid cease to innervate the cardiac and respiratory apparatus, so that death is preceded by sleep and stupor.

Local Effects of Cold.—Parts of the body are not infrequently frozen, and may be lost in consequence. The primary effect of cold upon the surface of the body is to occasion contraction of the superficial blood vessels. The contraction, however, eventually gives place to a paralytic dilatation, by which the blood entering the surface of the body in increased volume becomes chilled. If a part of the body freeze during the stage of vascular contraction, it appears white and feels cold and solid. If, on the other hand, it freeze during the stage of vascular dilatation, it appears leaden and swollen and feels hard and cold.

The outcome of freezing will depend upon its duration and the extent of the cellular disorganization. If the freezing be superficial and no damage is done to the blood vessels the part may recover perfectly, and many persons have had their ears freeze in severe weather without very serious consequences. If, however, the consolidation of the tissues descend more deeply, and the blood vessels are affected and their walls damaged, and many of the cells of the part disorganized, the death of the part, or gangrene, sets in. Such gangrene will be moist or dry according to the blood content of the part.

It is during the thawing of the frozen part that the re-entrance of blood manifests the vascular and other disturbances present. It is popularly, though perhaps erroneously, supposed that frozen parts should be slowly thawed, so as to prevent too violent a reaction and an increased vascular disturbance. It is, however, probably true that the disturbance is already complete, but only appears when the part again softens, and no exercise of care can prevent it.

Electricity is capable of damaging the body either through the heat generated or through the resistance to its passage through the body. Electric burns are usually deep and destructive, and are accompanied by considerable shock.

Powerful electric currents may occasion death through the resistance the body offers to their passage. Lightning stroke operates in the same manner. Either lightning or artificial electricity causes death when powerful enough; or produces a shock, followed by more or less injury to the nervous system, when less potent; or causes a disagreeable shock, with muscular contraction, etc., if still less powerful.

In death from lightning stroke, peculiar purplish arborescent markings early appear upon the surface of the body, but disappear later.

X-rays appear to be distinctly destructive to the body cells when exposure to them is prolonged or frequently repeated, when high-vacuum tubes are employed, and when the tube is held close to the skin, but Codman estimates the chances of *x*-ray burns to be less than 1 in 10,000. The form of burn most frequently seen is called "skiagraphers' dermatitis," and occurs chiefly on the face and hands of *x*-ray workers, tubemakers, and exhibitionists. The skin first appears chapped, then hypertrophic, and is wrinkled, fissured, and cracked.

In more mild cases the nutrition of the nails is seriously modified, so that they become deformed, striated, and brittle. When a little more severe, blebs, exfoliations of epidermis, and loss of the nails result, and the nutrition of the part becomes so disturbed that healing is slow. More severe cases may progress to ulceration, sloughs, extending so deeply as to expose the tendon sheaths and joints, sometimes forming.

In the accidental cases occurring in those subjected to single exposures, the lesions resemble burns of the first, second, and third degrees.

Rare cases of burns or lesions of internal organs have been recorded, but

Gilchrist, Scott, and Codman all find the evidence of their actual existence quite doubtful.

The pathology of the lesion is obscure. It is, however, supposed to depend upon injury of the trophic nerves of the part, because the lesion is delayed in its appearance, is progressive in character, and fails to react to stimulating treatment. Microscopically the lesions resemble those of inflammation.

Becquerel's rays, discovered in 1896 by M. Becquerel, are given off from certain radiant substances, such as uranium salts, radium, pitch blend, chaleolite, antunite, cleveite, monagite, and other minerals. The rays are luminous, actinic, and skiagraphic. They also render the air through which they pass a conductor of electricity. The prolonged action of these rays upon the skin, as when radiant substances are carried in the pocket, may produce burns somewhat similar to those caused by *x*-rays. The skin is hard, swollen, and painful from erythema, desquamation, and chronic ulceration. The burns may persist for months.

Light.—The exposure of the retina to any intense light, such as that of the sun or the electric arc, calcium, or acetylene lights, and even ordinary gas, incandescent, and lamp lights, is very destructive to sight from the occurrence of acute retinitis.

Light also affects the pigment deposition in the dermal cells. Exposure to the sun causes tanning and freckling, and may even produce an acute dermatitis with vesication. Electric lights may produce a similar effect, but do so only when the exposure is prolonged and the object in close proximity.

Sounds have an influence upon the health to a more considerable degree than might at first be imagined. Excessive atmospheric vibrations, such as accompany the discharge of cannon, may cause considerable distress of the organs of hearing. Constant noise, as in boiler and machine shops, causes permanent deafness. Persistent confusion of sounds, such as characterize the bustle of a great city, with occasional outbursts of fire, ambulance, and police patrol bells, etc., are said to predispose to neurasthenia.

Atmospheric pressure probably exerts very little, if any, influence upon animals in their normal environment, for the reason that they have during their entire existence adapted their structure to the normal pressure. Changes of altitude, however, early show their effects either through rarity or increased pressure.

1. *Diminished atmospheric pressure* is experienced by all who ascend high mountains or make balloon ascensions. The lips first become livid, then blue; there is more or less dyspnea and some nervous excitement. Faintness, hemorrhage, and vomiting may occur. The condition is commonly known as "mountain sickness."

Diminished atmospheric pressure increases the number of red corpuscles in the blood, with corresponding increase in their specific gravity and hemoglobin content. These changes develop in a brief time and persist after return to ordinary altitudes.

2. *Increased atmospheric pressure* is experienced in diving-bells and suits. The symptoms consist of ringing in the ears, bleeding from the nose, ears, and other mucous membranes, delirium, and sometimes palsy. Degeneration and vacuolation of the cells of the central nervous system have been found. The untoward symptoms make their appearance upon rapid return to the normal atmospheric pressure. The condition is commonly spoken of as "caisson disease."

Season has its effect upon disease. During the winter months the hospitals fill up with pneumonia cases, the dispensaries with laryngitis, bronchitis, etc. Diphtheria also occurs throughout the winter rather than throughout the summer. With the advent of spring typhoid fever and malaria make their appearance, persisting during the summer and autumn. In the summer yellow fever, malarial, and diarrheal diseases are more frequent than at any other season. The explanation of some of these diseases and their relation to seasons is easily made. Thus, malarial and yellow fever depend upon certain mosquitoes, and occur only during the seasons in which they are active. Diarrheal diseases of infants during the summer depend in part upon micro-organismal pollution of the milk ; those of adults partly upon green fruits, partly upon such parasites as Amœba coli.

Climate has such a far-reaching influence upon health and disease that climatology has become an important study in recent years. The features to be considered as bearing upon disease are the latitude, altitude, character of the soil, proximity to bodies of water, the number of trees, and the prevalence of winds and rains.

The adaptability of the human being to his environment has, through the aid of buildings protecting him from the weather, fires maintaining the temperature, and clothing to cover the body, enabled mankind to overcome the rigors of climate, so that latitude has ceased to be an exciting cause of disease.

Exposure to cold in Arctic climates may cause death by freezing, or the loss of parts from gangrene following freezing. Pneumonia is common in cold climates and cold seasons. The cold, by causing the members of a family or community to huddle together and live in close relationship to their domestic animals, favors the spread of diseases communicated from individual to individual or from animal to man.

In hot climates, especially when humid, parasitic and epidemic diseases are frequent. Gastro-intestinal diseases also prevail. Excessively hot, dry climates frequently produce heat stroke and insolation. The exposure of the body necessary for comfort in hot climates predisposes to the occurrence of diseases transmitted by the bites of insects, and to dermal poisonings by insects, plants, etc.

Temperate latitudes are shown by the prosperity of the human race occupying them to be best adapted to the requirements of mankind.

The effect of altitude has been considered under the head of Atmospheric Pressure.

Moist atmospheres seem to predispose to tuberculosis. Moist, cold climates appear to predispose to rheumatism.

The telluric influences are marked, those regions appearing to be most salubrious in which a loose soil readily drains away the rain water.

Trees are extremely useful because of the evaporation of water that they occasion, which dries the soil and discharges some moisture into the air. They also utilize the CO_2, and thus continually purify the air.

The peculiar geographic distribution of certain diseases usually depends upon the presence or absence of their specific parasites in certain areas. It may, however, depend upon the manners and customs of the people.

Intoxication.—A *poison* is a definite chemical substance of which small quantities are capable of exerting an injurious effect upon the functional or structural integrity of the organism.

Such substances may be formed within the body by its own metabolic processes and accumulate in injurious proportions through failure of the usual physiologic mechanisms for their destruction or elimination, or, as is more frequently the case, may be introduced from without. The first condition occasions what is described as *autointoxication*, *autochthonous* intoxication, or *endogenous* intoxication ; the second, *exogenous* intoxication.

Autointoxication results from the injurious action of substances produced by the metabolic processes of the body itself.

In the metabolism of the body such substances are constantly being formed, the only reason they pass unnoticed being the ready excretion that they meet through the eliminative organs. (In the section upon Metabolism this subject will be treated at some length.)

Autointoxication may depend upon:

1. *Faulty elimination* of excrementitious substances that accumulate in the blood and tissues. It usually makes its appearance in diseases associated with suppression of the urinary or cutaneous excretions and uremia.

2. *Excessive glandular secretion* is sometimes of ill effect upon the body, as may be the case in exophthalmic goiter with excessive absorption of thyroid substance.

3. *Irregular absorption* of digestive products may lead to disease. Thus, if the albumoses and peptones absorbed from the intestine fail to be transformed again to albumins by the cellular enzymes in their passage through the intestinal mucosa, their appearance in the blood causes intoxication.

4. *Incomplete chemical transformation* of the nucleins, that, instead of progressing to the formation of urea, yield xanthin, hypoxanthin, adenin, etc., causing leukomain-poisoning. Acetone may be imperfectly decomposed in diabetes, causing acetonemia.

Leukomains are basic chemical compounds, closely resembling vegetable alkaloids, produced by the metabolic activity of the organism. It is not improbable that some of them are produced by bacterial activity. The leukomains seem to be in part derived from the *nuclein* of the cells, and in part from *kreatin* from the muscles. The *nucleinic leukomains* are numerous, the most important being *adenin* ($C_5H_5N_5$), *hypoxanthin* ($C_5H_4N_4O$), *xanthin* ($C_5H_4N_4O_2$), *guanin* ($C_5H_5N_5O$), *heteroxanthin* ($C_6H_6N_4O_2$), and *paraxanthin* ($C_7H_8N_4O_2$).

These substances are closely related to uric acid, and have been called xanthin, alloxin, or purin bases, familiarly as the *alloxuric bases*. Cyanogen is shown in the chemical formula of nuclein and its derivatives, but its relation to them is not understood.

These leukomains are for the most part whitish amorphous or crystalline solids, forming neutral solutions in water, in which they are sparingly soluble. They are almost insoluble in ether. They have feeble combining powers with acids and alkalies.

It is not known how definitely the leukomains are related to the production of disease, but the present tendency is to regard them as important factors in the affections included under what is known as the "*uric acid diathesis.*"

The *kreatinic leukomains* are closely related to those of the nuclein group. The principal members of the group are *kreatin* ($N(CH_3)CH_2COOH$), *kreatinin* ($N(CH_3)CH_2CO$), *arginin* ($C_6H_{14}N_4O_2$), *lysatin* ($C_6H_{13}N_3O_2$), and *lysatinin* ($C_6H_{11}N_3O$).

Exogenous Intoxication.—Exogenous poisons may be of *immediate* or *remote* action; that is, some of them at once act destructively upon the tissues with which they come in contact, while others must be absorbed into the blood and be carried to the particular structures upon which they act. Their operation may also be *indiscriminate* or *selective*, the former having a wide destructive effect upon many different tissue elements, while the latter act only upon a certain few cells that they may reach only after a circuitous route through the blood vessels.

Poisons of Immediate and Indiscriminate Action.—These embrace the *caustics* and *irritants*. Their effects are most marked where they first reach the tissues in greatest concentration. In some cases the effect is entirely local, depending upon immediate contact; but in other cases the local action is succeeded by the absorption of the poison and a later remote effect. The chief poisons belonging to this class are the caustic acids and alkalies, the salts of the heavy metals, especially mercury, zinc, silver, and antimony, a few vegetable substances, such as croton oil, mustard, rhus, and some animal products, such as cantharidin, venom, etc.

The lesions produced by each poison will be in proportion to its activity. Cantharides and mustard applied to the skin produce erythema, followed by vesication and necrosis. Croton oil produces a characteristic pustulation. The venoms vary in their effects; some, those of bees, wasps, and spiders, occasioning painful swelling; those of scorpions, centipedes, and tarantulas causing much more marked injury and destruction of tissue; those of serpents, especially the *viperidæ*, inducing extensive sloughs. Carbolic acid causes a whitish eschar to form upon the surfaces with which it is brought in contact; nitric acid destroys the tissues with which it comes in contact, staining them yellow; sulphuric acid oxidizes the tissues, covering them with a black pulp.

Some of these poisons with immediate and indiscriminate action are harmless or nearly harmless when diluted; but others, such as arsenic, phosphorus, antimony, and some of the venoms, have quite a marked remote as well as immediate effect, and when absorbed into the blood, especially in the case of phosphorus, cause widespread parenchymatous changes, with fatty degeneration of the liver, kidneys, and other organs.

In some cases the absorbed poison is hurried to certain organs for elimination, and occasions greater damage through this means than would otherwise occur. This is especially true of cantharides and its effect upon the kidneys.

Poisons of Remote and Selective Action.—The absorption of certain poisons into the blood is frequently followed by a *combination with hemoglobin*, by which the oxygen-combining power is destroyed. The combination most frequently formed is *methemoglobin*, isomeric with oxyhemoglobin but so stable that oxygen cannot be liberated in the tissues. The methemoglobin imparts a sepia-brown color to the blood. Methemoglobin is formed in poisoning by many of the coal-tar products, such as acetanilid, phenacetin, trional, and also by potassium chlorate, pyrogallol, dinitrobenzol, nitroglycerin, anilin oil, etc.

Poisonous quantities of carbon monoxid combine with hemoglobin to form *carbo-oxyhemoglobin*, that has a cherry-red color. A bright-red color is also imparted to the blood by hydrocyanic acid, depending upon *cyanhemoglobin*. *Sulphomethemoglobin* may follow inhalation of sulphuretted hydrogen.

Hemolysis also results from the direct action of poisons upon the blood, and is observed in intoxication from phenacetin, acetanilid, antipyrin, trinitrobenzol, potassium chlorate, arsenated hydrogen, venom, phallin, etc.

Coagulation of the blood may also be caused by the absorption or injection of ricin, abrin, alcohol, ether, heterogeneous serums, etc. Nearly all of these "blood poisons" have additional poisonous effects upon the organs.

One of the most interesting phenomena attending intoxication is that of *selective action*. This is apparently something more than the chronic irritation of those organs first receiving the absorbed poison, as is observed in cirrhosis of the liver following chronic alcohol and lead intoxication; or the result of elimination, as in bichlorid of mercury, lead, and cantharides elimination, in which the kidneys are affected, but bespeaks some actual chemical affinity between certain cells or groups of cells and the toxic substance. Thus, one of the poisons in serpents' venom is markedly injurious to the respiratory center. Lead, when taken into the system for any length of time in small quantities, causes "wrist-drop" from a form of peripheral neuritis. Diphtheria toxin selects the peripheral nerves for its activity, and causes neuritis and palsy. Curara acts solely upon the motor nerves. Tetanus toxin acts upon the muscles direct to produce the tonic spasms, and upon the motor cells of the cord to produce the clonic spasms. Strychnia stimulates the respiratory center and excites the motor nerves of the spinal cord. The bromids and chloral depress the same cells. Caffein, digitalis, spartein, strophanthus, etc., act in various ways upon the cardiac innervation. Nitrite of amyl and other drugs relax the vasomotor nerves; adrenalin stimulates them.

These illustrations might be continued almost indefinitely, but enough have been given to show how remarkable is the activity of certain substances upon specific cellular groups. It is, indeed, a knowledge of these specific actions of poisonous substances that forms the foundation of therapeutics, and it is only a thorough knowledge of their pharmacology that gives medicine a firm scientific station.

Food may, through its excess, deficiency, innutritiousness, or unwholesomeness, act either as an exciting or predisposing cause of disease. The pathologic states to which these abnormalities give rise will be considered under the Disorders of Digestion (*q. v.*), so that at this point it may simply be stated that lack of food and innutritious foods predispose to weakness, atrophy, marasmus, and starvation. Excess of food is apt to occasion gastro-intestinal disturbances unless it happens that the digestive organs are able to dispose of what is consumed, when the tendency will be toward obesity.

Foods are regarded as unwholesome when indigestible, when their nutritiousness is below the adopted standard, and when chemical changes, such as decomposition or putrefaction, cause them to become irritating or poisonous.

Food poisons usually depend upon the activity of fungi. Rye may become poisonous through the growth of the *ergot* ("spurred rye"). Corn is rendered unfit for use by the "blight," a fungous growth. Bacteria, by their growth in proteid foods, sometimes produce ptomains that may be responsible for serious symptoms following the ingestion of the food. Not many ptomains are important in this way, but *tyrotoxicon*, that seems to be responsible for "*ice-cream poisoning*," must be mentioned. It is not known upon what particular bacterium the formation of tyrotoxicon depends. *Botulism*, a form of meat-poisoning sometimes observed to follow the use of improperly preserved meats, is caused either by Bacillus botulismus or ptomains it elaborates. Both forms of intoxication are characterized by vomiting, diarrhea, weakness, and collapse, and may terminate fatally. It is not impossible that some of the cases of enterocolitis of children are but cases of tyrotoxicon-poisoning. Cases of botulism may resemble typhoid fever.

Oysters and other shell-fish may at times become infected and probably diseased, and cause poisoning, when eaten, characterized by peculiar paralytic symptoms. From such oysters Brieger isolated a ptomain called *mytilotoxin*.

Foods may also be prejudicial to health because of parasites which they contain. Meat from diseased animals of all kinds should carefully be avoided, as, unless the cooking be very thorough, it is not impossible that infection may occur through the gastro-intestinal apparatus. Still more attention should be paid to milk as a possible vehicle of infection for the tubercle bacillus.

In the flesh of various animals encysted worms—cysticerci, trichinæ, etc.—may be present, making it imperative that butchers be constantly on guard and a regular meat inspection carried on to prevent the use of such flesh.

This infection with encysted worms extends to fish, the largest of all tapeworms, the Bothriocephalus latus, probably entering man from the flesh of the pike and other fishes in which it is common.

Environment.—*Occupation* is a most important predisposing cause of disease, its influence being exerted in many different ways.

1. *Physical Exertion.*—*Inactivity*, *indolence*, and *sedentary occupations* are associated with loss of the muscular movements essential to healthful circulation and vigorous respiration, and fail to stimulate the digestive organs to free action. Disuse of the muscles also leads to atrophy and consequent inability to use them actively. All disused parts atrophy. Sedentary occupations also occasion certain pressure symptoms, as when from interruption of the pelvic circulation hemorrhoids occur. The position of shoemakers, tailors, clerks, scholars, and others may, by exercising certain muscles and failing to exercise others, occasion various moderate deformities; as, for example, the eversion of the costal margins from the upward pressure of the abdominal organs in those who habitually stoop forward while sitting at desk or table.

Excessive activity and *overexertion* are more injurious, however, than inactivity. The muscles of the athlete and laborer undergo compensatory hypertrophy and call for increased nutriment. The demands upon the circulation in excessive muscular action are such that the heart is obliged to co-ordinate its activity with the demands made upon it, so that hypertrophy is inevitable. The entire individual is thus adjusted to meet the requirements of his physical efforts up to a certain point, and no ill effects result. If, however, the demands upon an inured physique are out of all proportion, as in such excessive exertions as "six-day go-as-you-please races," etc., the muscular tissue of the heart may be seriously and permanently damaged.

When the muscular exertions are violent and spasmodic, as is apt to be the case with porters, expressmen, deliverymen, and baggagemen, the sudden increase of blood pressure incident upon the violent exertion may cause minute cracks or fissures in the blood-vessel walls, with injury and thrombosis of the vasa vasorum, thus paving the way for the circumscribed form of arteriosclerosis and predisposing to aneurysm. If the vessels be diseased already, such sudden elevations of the pressure may cause rupture, with apoplexy, interstitial hemorrhages, etc. It is even possible by a sudden violent muscular exertion to lacerate a valve of the heart or rupture the wall of the aorta.

2. *Exposure.*—Exposure to the direct rays of the sun is chiefly to be feared when the atmosphere is particularly humid, so that free evaporation from the skin is prevented and the temperature of the body cooled. It is then that "heat exhaustion," a profound depression of the vital powers with depressed temperature, and "sunstroke" or *insolation*, a sudden attack of hyperthermia with delirium and profound prostration, make their appearance.

Occupations that bring men into exceptionally high artificial temperatures for considerable periods, as in stoking furnaces, baking bread, casting steel, etc., are usually associated with an unusual degree of activity of the skin. When such persons go into a cold atmosphere, the sudden chilling of the surface of the body, with the determination of the blood toward the internal organs, may result in serious disturbances of the lungs, kidneys, and other organs. Acute congestion of the lungs and acute nephritis have been thus occasioned.

Exposure to all kinds of weather promotes pulmonary diseases, and the necessary exposure attending ordinary pursuits during the winter months usually fills the hospitals with cases of pneumonia and other respiratory diseases.

Exposure to severe winter weather is apt to result in "frost-bite" and "chilblain," and may terminate in gangrene.

3. *Trauma.*—Contact and injury from foreign substances may lead to serious disorders. Aside from the numberless contusions, lacerations, inci-

sions, etc., suffered by workingmen, the action of certain substances upon their skins, eyes, respiratory and digestive organs are not to be forgotten. Coal miners are repeatedly struck by minute fragments of coal, that often bury themselves beneath the epidermis and remain as permanent disfigurements. Miners are said to suffer more frequently than other persons from a peculiar little fatty growth of the corneoscleral margin, and known as a *pinguecula*, from the traumatic lesions of the eyes. The inhalation of coal dust is succeeded by anthracosis or fibrosis of the lung, depending upon the chronic irritation of the inhaled dusts. Contact of the tissues with soot, paraffin, and tar is said to lead to epithelioma. The continued trauma of the muscles resulting from horseback-riding, drilling, etc., leads to *myositis ossificans*.

4. *Intoxication.*—Many poisonous substances utilized in the arts react disastrously upon those handling them. Chief among them are lead, arsenic, phosphorus, and mercury. It is surprising to see in what a variety of ways lead-poisoning can occur; thus, it may depend upon the inhalation of the lead by those grinding and mixing paints; or by ingestion from the paint-stained, and hence lead-stained, fingers of painters. Plumbers and tinsmiths and roofers may derive it from the lead in pipes or the solder with which they work; seamstresses have been known to become poisoned by biting off colored threads brought in contact with lead solutions during dyeing.

Arsenic is used in many colors for printing wall papers, etc., and in vermin exterminators, medicines, etc., from all of which it may accidentally be inhaled or ingested and occasion poisoning.

Mercurial poisoning is observed in barometer makers, chemists, and electric-light bulb makers, who work with mercurial vacuum pumps, etc.

Phosphorus-poisoning is usually observed in match factories.

5. *Nerve Exhaustion.*—This is chiefly observed in excessive nervous tension and overwork. It sometimes manifests itself in general nervous depression, with intellectual confusion, loss of memory, loss of responsibility, fatigue, and malaise. It may, however, be more local in manifestation, affecting first certain nerves and motor areas before extending generally through the brain. This is seen in such occupation neuroses as writers' cramp, etc., where the particular member most used cannot longer be properly innervated and made to perform its functions.

Association of Man with Man.—All occupations that lead to overcrowding, as in the "sweat-shops," are detrimental because of the vitiation of the atmosphere, as well as because disease germs are so apt to be passed from one workman to another. Tuberculosis becomes in this way the dreaded scourge of the tenement districts.

As this crowding is chiefly among workmen of the poorer classes, and as such workmen are apt to be ignorant, careless, and dirty, parasites abound among the crowded—bacteria, protozoa, worms, insects, etc., all coming in for their place.

Every form of contagious disease is favored by intimate association of man with man, and all occupations requiring the close confinement of numbers of persons in limited space should be carefully supervised in order that tuberculosis, leprosy, syphilis, etc., be guarded against.

The innocent transfer of syphilis from individual to individual is not infrequently brought about by the use of tools, etc. Thus, in glass factories a pipe for blowing bottles, lamp chimneys, etc., is often passed from man to man as the different stages of the work are accomplished, the infectious virus from a mucous patch in the mouth of one man being transferred to his healthy and innocent neighbor.

The common use of toilet articles by a number of men and women is not without danger from infection, as towels may be infected with gonococci by the fingers of one person, and the organisms so transferred to the eyes of others. Parasitic scalp affections may also be transferred from man to man by the use of combs and brushes. In public eating-houses the badly washed knives, forks, and spoons may transfer syphilitic or tuberculous virus from man to man, while the cups at public drinking-fountains may do the same.

By sexual contacts, though also occasionally by innocent personal contacts, and rarely by fomites, the venereal diseases—gonorrhea, syphilis, and chancroid—are communicated from one to another individual.

Association of man and the domestic animals may result in the communication of diseases. Thus, those who are constantly brought into contact with horses, as jockeys, hostlers, cavalrymen, etc., sometimes become infected with glanders.

Butchers and veterinary surgeons occasionally inoculate themselves with tuberculosis from animals they dissect.

Plague is recognized to be primarily a disease of the rat, first making its appearance where poverty and crowding, filth and rats are associated.

Psittacosis, an epidemic pulmonary disease of parrots, has on several occasions been transmitted to man with resulting fatal epidemics. In one such epidemic in France 70 persons were affected, with 34 deaths.

Cow-pox was first observed as a contagious disease upon the fingers and hands of milkmaids and dairymen, resulting from contact with diseased cows' udders.

Hydrophobia, an infectious disease of the lower animals, especially of the canine animals, is usually transmitted to man through the bite of a dog.

Parasitic and suctorial insects which prey upon the lower animals sometimes also turn upon man, transferring to his skin or tissues the parasitic organisms they have taken up.

Higher parasites, especially parasitic worms, sometimes have their adult existence in the lower animals and their embryo existence in man, or *vice versâ*. The result is that where man and the lower animals live in close association, the ova of these parasites are more easily transferred from one to another than under other conditions. Thus, the Esquimaux, who live in most intimate relation with their dogs, are said to suffer more than other peoples from the *Tænia echinococcus*. In parts of Europe in which dogs are held in high esteem as household companions the tapeworm is most common. In America, where greater cleanliness is observed and dogs are given their proper place in the household, this parasite is scarcely known.

The *trichophytons* are probably in large measure derived from the lower animals, which are not infrequently affected.

Contact with wild animals may be followed by serious results to man. Aside from their ability to do physical harm because of size, structure, irritability, etc., certain animals are provided with devices for introducing poisons with marked destructive effect upon the tissues. Such venom apparatus may be in the head, the poison being introduced through wounds inflicted by the teeth, as in the serpents, centipedes, and spiders; or may be at the tail, the instrument of injection being a modified ovipositor, as in the scorpions, bees, and wasps. Other animals are provided with cutaneous venoms for offensive purposes, as the toad, certain salamanders, and certain myriapods, as Iulus terrestris. Still other animals, as the polecat, possess mephitic glands, usually situated near the anal orifices and sexual glands, that secrete an extremely disgusting fluid whose physiologic effects upon small animals may be marked, though only disagreeable to man.

The quantity of these organic poisons necessary to do injury varies with their quality.

The best known are those of the hymenopterous insects and serpents. In a number of cases a single wasp or bee sting has caused death. It is estimated that in India no fewer than 20,000 human beings succumb each year to the bites of venomous serpents. Of the serpents, the cobras and vipers are the chief venomous forms. The venom contains several injurious principles, one of which appears to act upon the respiratory nerve centers, another upon the blood, and a third upon the tissues with which it comes in contact, causing necrotic changes, destruction of the small blood vessels, hemorrhagic extravasations into the damaged areas, and a marked predisposition to infection, and a fourth principle that destroys the germicidal action of the blood.

Wolves, wildcats, skunks, and other wild animals may also suffer from rabies, in paroxysms of which they make delirious attacks upon human beings, snapping and biting and thus transmitting rabies to them.

Parasitic diseases of the wild animals may be transmitted to man through the intermediation of suctorial insects, and may also sometimes probably be transmitted to man. Thus, the trypanosome disease of South Africa known as *nagana* or "tsetse-fly disease," and the Indian "surra" or cattle plague, occur only when certain flies (Glossina morsitans in the case of nagana) are present to convey the parasites. Nagana makes its appearance in a locality only when big game pays it a visit.

CHAPTER II.

DEFECTS OF DEVELOPMENT.

Any departure from the normal embryonal developmental processes leads to a subsequent structural defect known as a *malformation*. Some, that regularly recur in the same form and probably depend upon similar causes, are described as *typical*, others as *atypical malformations*. Every variation may occur, from defects so trivial or concealed as to pass unnoticed, to absence of parts essential to life.

Grossly malformed individuals are called *monsters*. The malformations may include structural defects of a single individual, of a partly divided individual, or of two or more united individuals. The partly divided individuals and the united twins and triplets are known as *double* and *triple monsters*.

Malformations are serious according to degree. Thus, a harelip may be unsightly, interfere somewhat with sucking in babyhood, and necessitate surgical remediation, but cannot be called a serious deformity; spina bifida resulting from rachischisis is sooner or later fatal, either from rupture of the cyst and loss of cerebrospinal fluid or infection; while congenital absence of the heart is incompatible with extra-uterine existence.

Many causes lead to malformation, but few are fully understood. They are usually divided into *internal causes*, that exist in the germ itself, and *external causes*, that act upon the developing embryo from without, and by pressing upon it, forming adhesions to it, etc., distort its developing parts. The external causes probably less frequently occasion malformations than might be supposed, as, when serious, they usually occasion the death of the embryo.

It must be understood that the causes that are to bring about serious malformations must operate upon the embryo while it is very young and in a stage of development adapted to modification. The greater number probably occur before the third month. The operation of external forces in later fetal life produces conditions resembling those acquired after birth, though the difference in environment explains the variations. Concerning the intrinsic causes that operate to produce monsters during the first three months of embryonal existence, we are acquiring more and more information as the result of experimental work upon the ova of invertebrate and occasionally upon vertebrate animals. Thus, it is now known that by jarring, rotating, and transposing the egg during its early segmentation definite monstrous developments can be determined.

I. **Single Malformations.**—These occur in single individuals, and may be divided as follows:

(*a*) **Depending upon Intrinsic Causes.**—1. **Aplasia,** or complete failure of development, may be general or local. If general, the cessation of development is followed by the death of the embryo and its expulsion as an *abortion*. In some cases, however, the products of conception are retained and absorbed in part; the remainder, usually the membranes, forming fleshy masses known as *moles*. The chorion sometimes degenerates in a peculiar manner, by which its villi become cystic and the whole thing forms a mass similar to a bunch of grapes. This is called a *hydatiform* or *hydatidiform mole*.

Instead of being absorbed, the embryo, especially in abdominal pregnancies, sometimes becomes incrusted or impregnated with mineral salts and forms what is known as a *lithopedion*. Small calcified fetuses may be carried about in the abdominal cavity for years and still perfectly retain their external configuration.

Local aplasia manifests itself in the congenital absence of parts of the body—fingers, toes, limbs, and internal organs. Its importance depends upon the relation of the aplastic organ to the general vital condition. In the acephalic and acardiac monsters the developmental defects are necessarily incompatible with life.

Failure of some or all of the limbs to develop, with resulting *amelus*, is an important and familiar form of aplasia. It must, however, be carefully differentiated from the intra-uterine amputations that sometimes occur in consequence of amniotic adhesions and bands pressing upon and ligating the developing limbs.

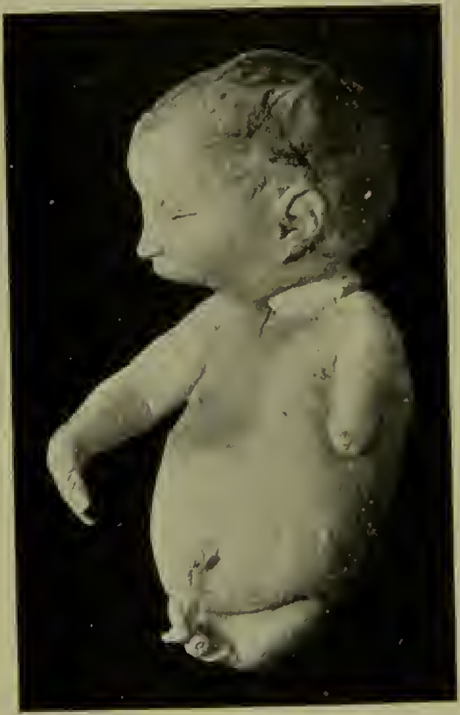

FIG. 1.—Agnathus ectromelus apus (Lewis).

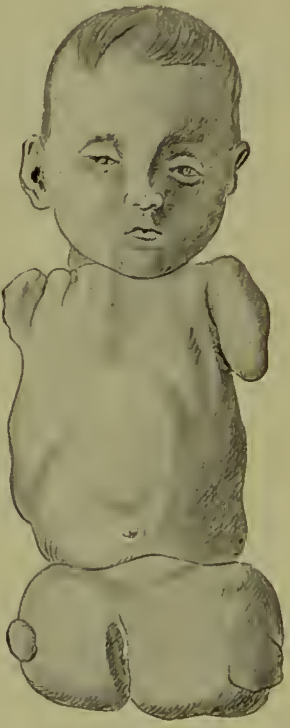

FIG. 2.—Amelus (Ziegler).

2. **Hypoplasia.**—Failure of organs and members to attain their full size is a common defect. Thus, a large, well-developed kidney upon one side of the body is sometimes accompanied by a mere rudiment of the corresponding organ of the other side. Sometimes the extremities of the body are hypoplastic, and, with a large head and body, only rudimentary limbs are present, as in *micromelus*. Aplasia and hypoplasia are responsible for many of the cases of *congenital absence* of parts. Sometimes the entire limbs are absent (*amelus*) or abortive (*ectromelus*); sometimes single limbs are absent. Sometimes the limbs are absent but the hands and feet present, but directly attached to the trunk (*phocomelus*). Sometimes single bones of the limbs are absent;

sometimes the clavicles are absent. The congenital absence of internal organs also occurs, being particularly frequent in the paired organs, one of which may be absent or rudimentary, while the other compensatorily performs its function. Congenital absence of the genital organs may occur without any other malformation of the body.

3. **Schistosis,** or *incomplete union* of the fetal arches, is a common cause of deformity. It may be anterior, posterior, or lateral.

Anterior Schistosis.—Schistosis of the face may depend upon rudimentary development or incomplete fusion of any of the branchial arches. *Aprosomia* or *schistoprosopia*, a very rare deformity, depends upon hypoplasia of the first branchial arches, so that the face does not develop, and, where it should have appeared, only an irregular surface or fissure, with malformed eyes and nose, exists. Much more frequently the facial defects are less radical and affect the lips, upper jaw, and palate, producing the familiar "harelip" or *cheiloschisis*, the "cleft palate" or *palatoschisis*, or the combination of cleft palate, cleft upper jaw, and harelip, or *cheilognathopalatoschisis*.

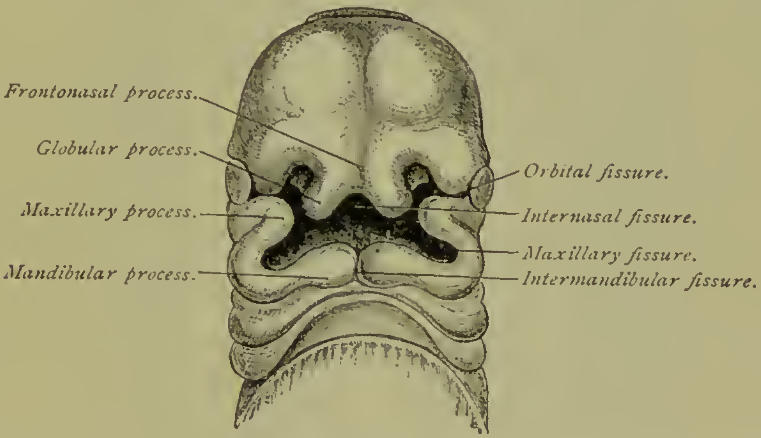

FIG. 3.—Head of an embryo, showing the disposition of the facial fissures (semi-diagrammatic) (Sutton).

The most frequent median defect is probably the divided uvula, which commonly passes unobserved.

Prosoposchisis is characterized by fissures passing from the mouth to the orbit either through the nostril, or across from the nostril to the orbit, or ascending obliquely from the corner of the eye, through the cheek, toward the canthus of the eye, dividing the maxillary bone externally to the canine tooth.

A fissure also sometimes extends from the corner of the mouth toward the temporal region, and is a cause of what is known as *macrostomia*. In very rare cases the mandibular tubercles fail to develop, and a deformity known as *agnathia*, or absence of the jaw, results. In the case described by Guardan the ears were conjoined beneath the palate (*synotia*).

Median fissures extending upward through the nose and upper jaw, through the symphysis mentis, and along the front of the neck are occasionally seen.

Incomplete fusion of the branchial clefts also leads in not infrequent cases to fistulous communications between the pharynx, larynx, or the trachea and the exterior. These are known as *fistulæ colli congenita*. By irregular though complete closure, with inclusion of surface or pharyngeal epithelium, the *branchial cysts* may be formed.

Incomplete union of the anterior thoracic wall (*thoracoschisis*) is very rare; it may lead to *ectopia cordis*. The abdominal wall is not infrequently defective in the umbilical and pubic regions. The omphalomesenteric duct, by which the intestine and the umbilical vesicle communicate, usually becomes occluded by the sixth week, but the abdominal wall is not perfected until the eighth week. The result is that the region of the umbilicus, which is the last to close, is apt to be the most imperfect part of the wall, and may by its defect lead to the formation of an *omphalocele* or *umbilical hernia* or *hernia funiculi umbilicalis*. In rare cases the whole abdomen may be open by a persistent central fissure (*gastroschisis completa*); and in still more rare cases both the thoracic and abdominal walls may be open (*thoracogastroschisis*). The abdominal walls in these cases are not separated from the amnion. The viscera lie in a sac composed of peritoneum and amnion. The peritoneum may also be absent; and it is sometimes observed that there is no umbilical cord, the umbilical vessels taking the shortest course to the placenta.

When the gastroschisis is low down in the pubic region an *extrophy of the bladder* or *ectopia vesicæ urinariæ* is very common. Not infrequently the bladder is as defective as the abdominal wall itself, and, being open in the anterior median line, inverts through the abdominal opening (*inversio vesicæ urinariæ*). The condition is not infrequently combined with the defective development of the penis by failure of union of its anterior surface, so that *epispadias* or *fissura genitalis* occurs.

In very rare cases the defect of the abdominal wall is accompanied by a defect of the intestine, usually in the cecum or colon, which becomes inverted, so that its mucous membrane projects from the parietal defect.

Von Recklinghausen has observed that clefts of the upper part of the abdominal wall are often combined with craniorachischisis, while defects of the lower part sometimes accompany myelocystocele. What relationship may exist between the two conditions is not known.

When the fissures resulting from schistosis occur about the sexual organs the cleft scrotum is of particular interest because of the resemblance to hermaphroditism. The fissure in the scrotum occupies the position of the raphe and extends backward, looking very much like the vulvar fissure, while the testicle on each side causes a prominence closely simulating the labia majora. If, as often happens, the testicles fail to descend, the resemblance to the female is generally increased, especially if the penis be small.

Posterior Schistosis.—When union of the arches forming the spinal column fails to take place, posterior schistosis or *rachischisis* occurs. The condition receives various names according to its position and extent; thus, if the entire spinal canal remains open, it is described as *holorachischisis* or *rachischisis totalis;* if only partly open, as *merorachischisis* or *rachischisis partialis*. This is the more frequent form of separation, and usually affects the sacrolumbar part of the spinal column. When the defect embraces both the spinal cord and cranium, as is commonly the case, it is called *craniorachischisis*.

When a case of *rachischisis* is carefully examined, it is usually observed that the defective tissue is of a bright-red color, and is covered by a peculiar velvety tissue closed in by a delicate integument, which may be in small amount or even wanting. "External to this tissue mass, which is not everywhere equally abundant, and which decreases at the sides, comes a delicate, transparent, vascular skin; next a zone of skin with epidermis, but somewhat thinner than the normal skin, and often bearing abundant hairs; then finally comes the normal skin." "According to von Recklinghausen, the soft red tissue mass is the malformed spinal cord, and is an extremely vascular tissue, containing often more or less abundant parts of the spinal cord, as nerve fibers, ganglion cells, and glia cells, and is, therefore, appropriately called the *area medullovasculosa.*" . . . . "The tegument upon which the area medullovasculosa lies is only the *pia mater*, which also continues into the red zone, which being also covered with epithelium is designated as the *zona epitheloserosa.*" "The prominent zone bordering this and covering the rudiments of the posterior vertebral arches is formed of cutis, and is known as the *zona dermatica.*"

Von Recklinghausen believes that rachischisis depends upon agenesis or hypoplasia of the dorsal ridges from which the vertebral arches are to be formed. The malformation of the spinal cord so marked in these cases is to be referred to the earliest developmental period, and probably results from underdevelopment of the blastoderm.

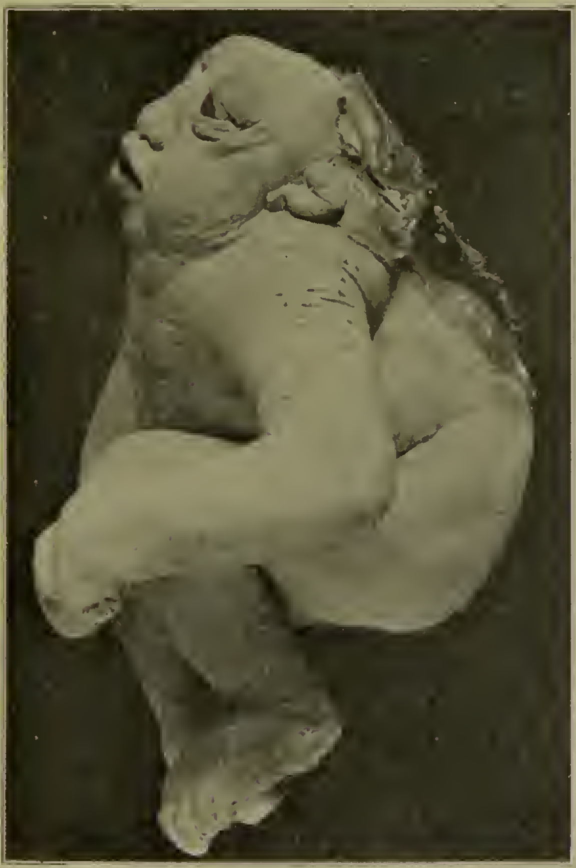

FIG. 4.—Anencephalia.

The chief deformities resulting from craniorachischisis and rachischisis are *anencephaly* and *spina bifida*.

Anencephaly, *acrania*, *cranioschisis*, and *craniorachischisis* occur in consequence of failure of the cranial bones to develop or to attain their full size, or because of abnormal openings between the cranial bones, through which hernial protrusions of the brain and its membranes occur and occasion subsequent atrophy of the bones. In some cases when the bones are present and formed, but the cranium for various reasons is extremely small, the term *microcephalus* is applied.

The most frequent condition is probably the craniorachischisis, in which

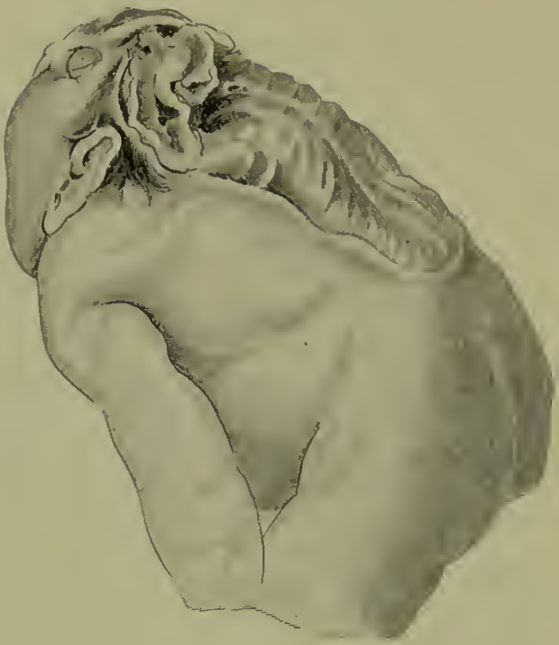

FIG. 5.—Craniorachischisis (Ziegler).

the upper part of the spinal canal and of the cranial bones fail to develop. The head may be very small and consist almost entirely of face. The

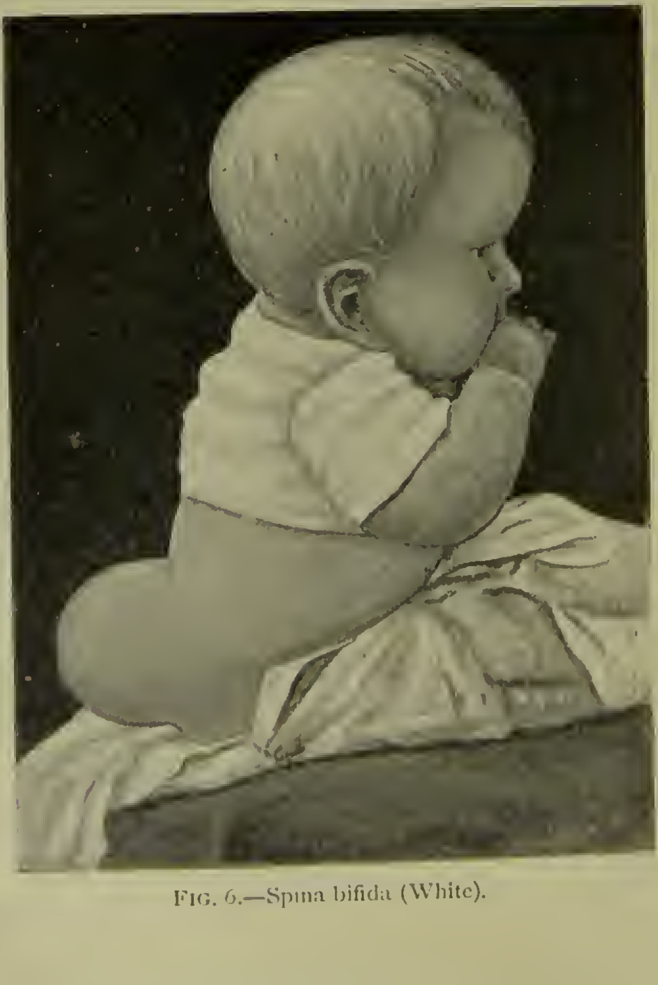

FIG. 6.—Spina bifida (White).

vault of the skull is lost, and is often represented by a concavity covered with the soft, red, velvety skin of the *area cerebrovasculosa*. The subjacent tissue may contain only scattered patches of brain substance. The head of the anencephalic monster is usually retracted and forms the area cerebrovasculosa, the red tissue continuing down the back a variable distance.

If no brain tissue can be found, the condition is described as *complete anencephalia*; when rudiments of brain tissue are present, as partial or *incomplete anencephalia*.

Through the defects in the cranium hernial protrusions of the membranes, or of the brain substance enclosed in its membranes, may occur. The purely membranous herniæ are called *meningoceles*; the cerebral herniæ, *encephaloceles*; combinations of both are called *encephalomeningoceles*. In rare cases parts of a ventricle may be included in the hernia, the condition being then called *hydrencephalocele*. By most authors anencephalic conditions are supposed to depend upon *hydrocephalus* occurring before the fourth month, but the depressed and inverted position of the remaining cranial bones has led others to think the condition depends upon some external pressure, such as might be caused by the cephalic cap of the amnion. Lebedeff thinks the condition depends upon an abnormally sharp curvature of the embryonal body, occurring when the end of the embryo has elongated abnormally or the cephalic envelope lagged behind in development. By this means the medullary plate is prevented from changing into the neural canal, or after so changing is destroyed. The cystic formations often found about the base of the skull are supposed to be fragments of the medullary plate included in the mesoderm.

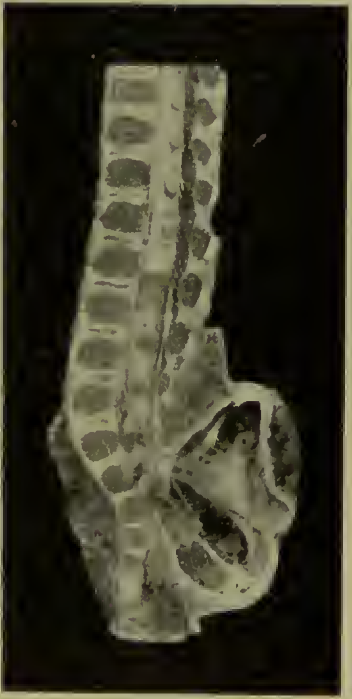

FIG. 7.—Spina bifida (meningomyelocele), showing cord and nerves crossing sac (Guy's Hospital Museum).

Ziegler is of the opinion that acrania is not always caused by the same factors, and, while in some cases Lebedeff may be correct, other cases probably depend upon adhesions to the cranial bones, and still others to aplasia of the cranial bones.

Hernial protrusions of the brain and its membranes usually occur in the occipital region, not far from the foramen magnum, but may also occur at the root of the nose, in the temporal region, the orbital fissure, and at the base of the skull.

Anencephaly is incompatible with life, and though such monsters may be born alive, they never live more than a few moments, probably because of the absence of the essential nervous ganglia of the base of the brain.

Spina bifida is a deformity resulting from schisis of the inferior part of the posterior wall of the spinal canal. The defective bony arches failing to support the weight of the contained cerebrospinal fluid cause bulging, and later hernial cystic protuberance, in the sacral region. Ordinarily the condition results in *myelomeningocele*, though *hydromeningocele*, *myelocele*, *myelocystomeningocele*, and *myelocystocele* may also occur.

As is usual in cases of rachischisis, there is evidence of an *area medullovasculosa*, though it is not rarely reduced to small patches of vascular tissue scattered about in the skin covering the tumor. The skin extends well up on the tumor and may cover it, and occasionally its surface is hirsute. The membranes of the cord are imperfect, and the dura mater is absent over the posterior surface of the cyst.

The mechanism of formation and morbid anatomy of the condition are very simple. The rachischisis permits fluid to collect in the subarachnoid space and form a local distention that causes the dura to atrophy, yield, and permit the formation of a sac in the subcutaneous tissues. The spinal cord is usually drawn posteriorly, and the nerve roots may pass through the sac or along its walls.

The names applied to the condition depend upon its anatomic structure. If it is simply a bulging of the distended membranes, it is called a *meningocele*, or a *hydromeningocele*, or a *hydrorrhachis externa circumscripta*. If the spinal cord be included in the hernial protrusion, it is a *myelocele* or a *myelomeningocele*.

In nearly all cases the hernia protrudes posteriorly, forming the ordinary *spina bifida* or *posterior meningocele*; but in rare cases it may protrude anteriorly, forming an *anterior meningocele*. The central canal of the spinal cord is sometimes dilated, and at the defective part of the spinal column causes the formation of a hernial pouch made up of the spinal cord and its membranes, this being known as a *syringomyelocele*, *myelocystocele*, or *hydromyelocele*.

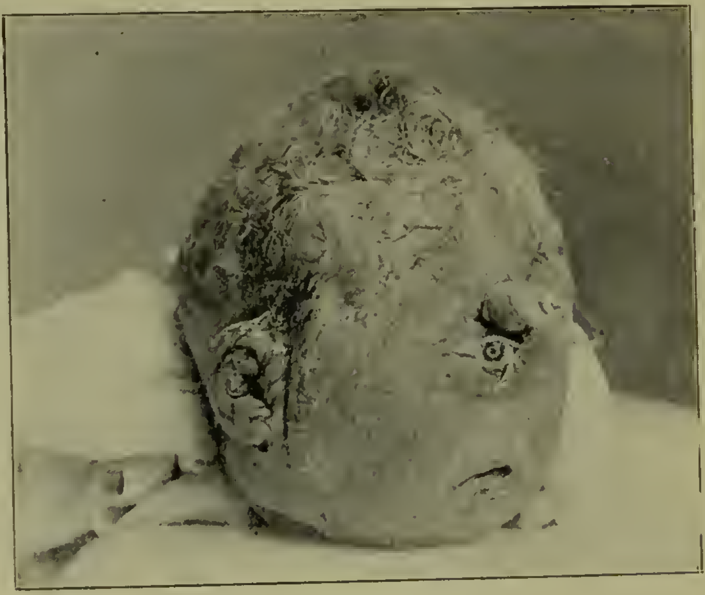

FIG. 8.—Cyclocephalus (Falk).

In some cases of rachischisis there is division or reduplication of the spinal cord as well as a defect of osseous union. This condition is probably dependent upon a faulty union of the elementary symmetric cord halves, not to actual duplications.

Spina bifida is a serious malformation that in the majority of cases destroys life by rupture following progressive increase in the size of the cyst and thinning of the coverings. The entailed loss of cerebrospinal fluid, together with the infections that are almost sure to occur, are fatal. Persons afflicted with the trouble sometimes live to adult life, but are subject to motor and other nervous disorders resulting from the pressure of the fluid accumulation upon the spinal cord and nerves, and from atrophy of the essential nervous elements.

4. **Synactosis,** or abnormal union of parts, is a less frequent cause of malformation than schistosis. It sometimes occurs in the form of an incomplete separation of parts that should normally differentiate; sometimes as a fusion of contiguous parts. Thus, in cases in which the anterior cerebral vesicle is hypoplastic, the development of the brain leads to the formation of a sac-like nervous mass filled with clear fluid. Or, if the brain is not so simple, portions of its tissue may be wanting, and the olfactory bulbs, the corpus callosum, some of the convolutions, etc., absent. The optic thalami are sometimes united. The corpora quadrigemina, pons, medulla, and cerebellum are usually not involved.

The anterior part of the skull may be markedly deformed, and there may be a single orbit containing a single eye or two imperfectly differentiated eyes. Such a monster is described as a *cyclops* (*cyclopia* or *synophthalmia*). The nose is usually also much deformed, and may be represented by a fleshy lump, usually situated above the eye (*arhinencephalia* and *ethmocephalia*). The ethmoid and nasal septa may be absent. Harelip and cleft palate are frequently associated conditions. The result of the bony deformities is that the anterior aspect of the head is extremely narrowed and may resemble a wedge.

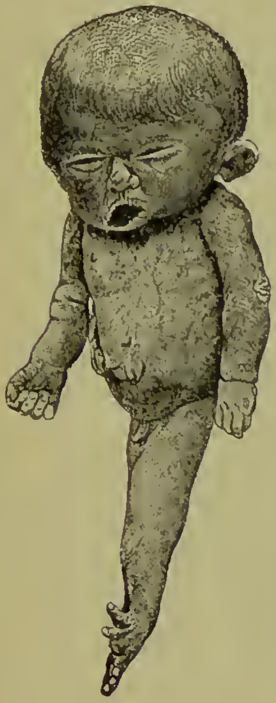

FIG. 9.—Sireniform fetus (Ballantyne).

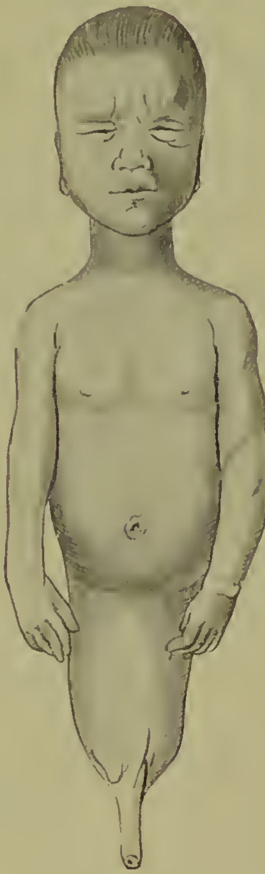

FIG. 10.—Sympus apus (Ziegler).

The limbs—*i. e.*, the lower limbs, sometimes coalesce, so that the individual terminates inferiorily in a conical extremity suggesting a mermaid's tail. This condition is known as *sympus*, *sirenomelia*, or *symmelia*. At the end of the sympus more or less deformed feet may be attached, the cases being subdivided into *sympus apus* (without feet), *sympus monopus* (with one foot), *sympus dipus* (with two feet).

More frequent are synactoses, or webbing of the fingers and toes (*pterodactylus*). Actually coalescent fingers and toes also occur (*syndactylus*). Fusion of the fingers is known as *perochirus*, as differentiated from *peropus*, or fusion of the toes. Such fusions are accompanied by more or less marked osseous fusion and deformity.

Under the caption of synactosis the imperforate anus and vagina and the various atresiæ might be mentioned, but in most cases it is difficult to determine whether they depend upon fusion of parts adjacent to them or cessations of development, so that they may be better treated under a separate heading.

5. **Multiplicitas membrorum** is not common except in those forms of malformation that can be properly included among the double monsters. Its most frequent occurrence is in the form of supernumerary fingers and toes (*polydactylus*). As many as ten fingers have sometimes been observed on one hand. It may in rare cases give rise to supernumerary ears, especially in the lower animals. Quite frequently one finds supernumerary internal organs, but usually in lobulated tissues, whose accidentally widely separated lobules may account for the phenomena. Thus, the pancreas is probably the organ most frequently accompanied by small accessory formations of similar structure, usually occurring near the chief organ, but sometimes in the wall of the stomach, and even in the anterior abdominal wall.

Supernumerary spleens are quite common, but nearly always occur in the immediate neighborhood of the spleen itself. Double ureters and pelves are common in the kidneys. The ovaries, testicles, and liver are rarely supernumerary.

Supernumerary mammary glands are not rare, as many as five having been observed upon a single woman; they are rare in men. They may be situated upon the thorax or abdomen or in the axilla. They have been seen in Scarpa's triangle and on the outer side of the thigh. Supernumerary nipples are more frequent, as many as ten having been observed in one case.

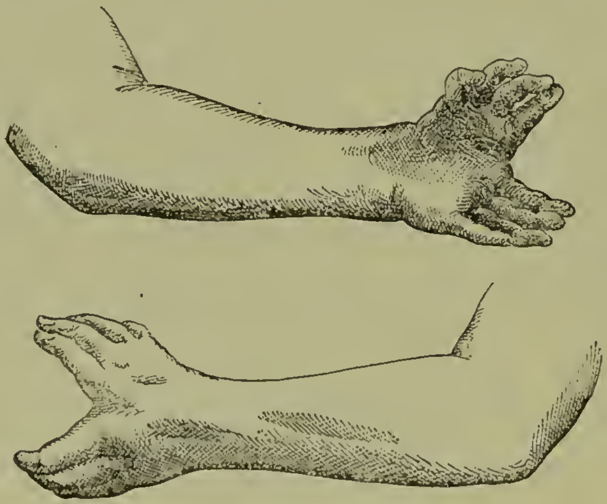

FIG. 11.—Double hand (Murray).

Supernumerary bones are not infrequent, the most frequent being extra ribs. When, as sometimes happens, there are supernumerary vertebræ, a true *tail* may be produced. Usually, however, the tail-like appendages seen in man are fleshy.

Duplications of the sexual organs are more common in the female than in the male. There may be two vaginæ or a septate vagina, two uteri or a bifid uterus (*uterus bicornus*), or a septate uterus. The occurrence of double vaginæ and uteri is easily understood when it is remembered that in the development, about the end of the second month of embryonal life, the two ducts of Müller and the Wolffian ducts fuse to form the uterus and vagina. The abnormalities mentioned depend upon variations in the perfection of this fusion.

In rare cases duplication of the penis has been observed, and in some of these cases both organs have been capable of performing the sexual act.

6. **Situs Abnormalis Viscerum.**—In very rare cases a true transposition of the viscera takes place. It is exactly the reverse of the position they

usually occupy. The heart is on the right side, the spleen also on the right side, the liver on the left side. There is, of course, no change in the paired organs.

Occasionally a kidney is loosely attached (floating kidney) and descends in the abdomen to the brim of the pelvis; or in a few cases a kidney is found situated and fixed in this position. Testicles may be retained in the abdominal cavity (*cryptorchia*) or only partially descend into the scrotum, remaining in the upper part of the inguinal canal (*ectopia inguinalis, cruroscrotalis, perinealis*, or *cruralis*).

Of all the viscera, the colon is most apt to depart from its normal type. Sometimes the cecum is small and short, barely descending to the iliac fossa; at other times it is long and dilated and hangs down over the brim of the pelvis. The ascending colon may be short, so that the transverse colon takes an oblique course across to the splenic flexure. The transverse colon is often long and may have a marked descent in the middle that can descend to the pubis or even into the pelvis. The sigmoid may be absent, or may be very large and variously formed.

Congenital luxations not infrequently occur at the hip, and sometimes at the elbow, knee, and shoulder. By some they are regarded as the result of arrested development of the acetabulum and head of the femur. The ligamentum teres is nearly always intact.

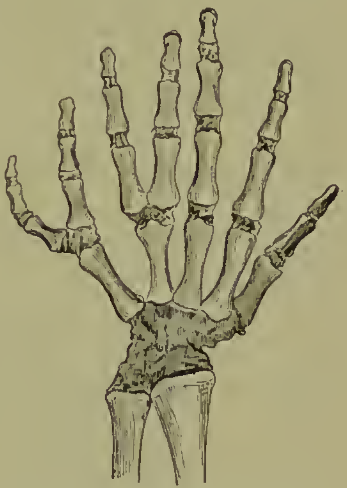

FIG. 12.—Supernumerary fingers (Ziegler).

Club-foot (talipes) may depend upon irregularities of development or upon nervous influences that lead certain muscles to predominate in action over others with which they should maintain a definite balance. Though the condition is sometimes present at birth, it usually does not complete its development until the period of walking is reached. The various forms are:

Talipes equinus, the heel being drawn up and the body supported on the toes.

Talipes calcaneus, the toes being elevated, the subject walking on the heel.

Talipes cavus or *arcuatus*, in which the foot is highly arched, and only the heel and toes touch the floor in walking. The foot is much shortened.

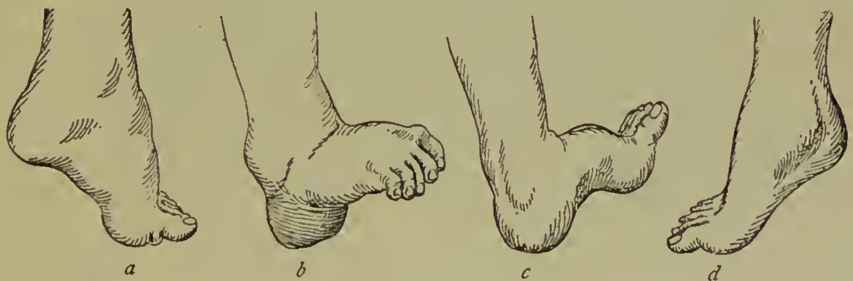

FIG. 13.—Varieties of clubbed feet: *a*, Talipes equinus; *b*, talipes calcaneus; *c*, talipes cavus or arcuatus; *d*, talipes equinovalgus.

Talipes varus, in which the outer side of the foot only touches the floor.

Talipes equinovarus, in which the outer side of the toes are walked upon.

Talipes calcaneovarus, in which the outer side of the heel is walked upon.

Talipes valgus, talipes equinovalgus, talipes calcaneovalgus, in which the inner side of the foot, the inner side of the toes, the inner side of the heel, respectively, are walked upon.

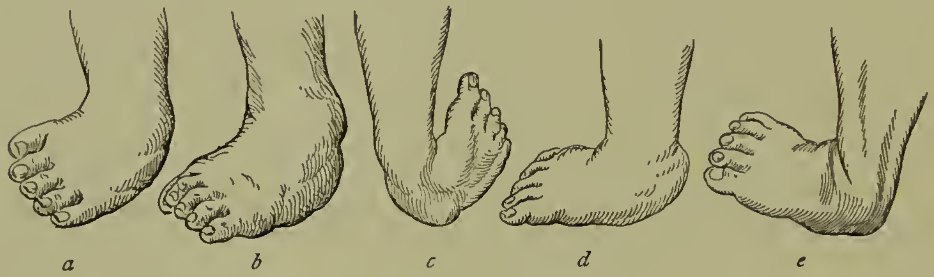

FIG. 14.—Varieties of clubbed feet: *a*, Talipes equinovarus; *b*, talipes varus; *c*, talipes calcaneovarus; *d*, talipes valgus; *e*, talipes calcaneovalgus.

Clubbed hands or *talipomanus* are much less common, and are usually occasioned by congenital deformity of the bones of the forearms.

7. **Congenital Obstructions.**—The mouth is in some cases abnormally small (*microstoma*) as the result of excessive union of the tissues of the maxillary and mandibular arches.

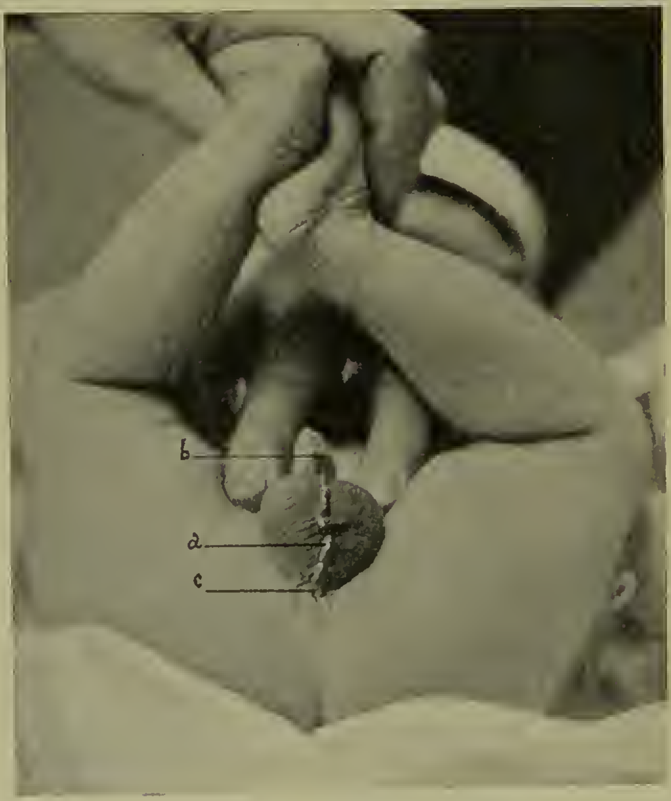

FIG. 15.—Malformation of the anus. Enterodeum (hindgut) continued as a tapering, tortuous tube (*a*) along the raphe of the scrotum, and ending by a minute opening (*b*) discharging meconium near the end of the penis; *c*, anal depression—imperforate (Peters).

The prepuce may be congenitally absent, and when present may be abnormally elongate and constricted at the orifice. When the orifice is extremely small the urine may meet with a marked obstruction to its escape, and dilatation of the bladder and ureters, and even hydronephrosis, may result from the backward pressure. When the orifice is so small that the prepuce cannot be drawn back over the glans penis, the condition is described as *phimosis*.

Urethral atresia may occur in both sexes. If the urine cannot escape, it collects during fetal life in great quantities in the bladder, which becomes as large as the entire abdomen of the fetus. Abnormally narrow urethra or hypertrophy of the colliculus seminalis may interfere with the escape of urine, but not to nearly the same degree.

The urethra may be absent in girls, the bladder opening into the vagina and preventing the serious results observed in atresia.

Atresia vaginæ becomes a serious impediment to the sexual act in adult life. *Atresia uteri* makes conception impossible, but both conditions are also serious in that they lead to retention of menstrual blood and secretions, which may cause distention of the uterus and consequent suffering.

Atresia ani or, as it is more frequently called, *imperforate anus* is not infrequent, and depends upon the failure of the rectum to grow down and unite with the anal tissues, to which it is often united by a fibrous cord. In these cases the rectum may terminate blindly (*atresia simplex*) or it may communicate with the vagina or urethra (*atresia ani vesicalis*, *urethralis*, or *vaginalis*).

8. **Persistent fetal structures** may lead to subsequent pathologic conditions by the growth of their cells to form tumor-like masses, or, as is more frequently the case, by the retention within them of fluids, so that cystic dilatation follows.

The *thyrolingual duct* sometimes imperfectly closes, and in after-life forms a cyst in the front of the neck. Or, if there remains an external communication, a fistula or sinus may exist in the front of the neck, from which a clear fluid or a mucous secretion escapes.

The *urachus* or urinary canal of the embryo, formed by prolongation of the fusiform vesicle formed by the dilatation of the embryonic portion of the allantois, sometimes remains open near the umbilicus, sometimes near the bladder, sometimes only in the middle portion, under which condition the accumulation of fluid, extending into its cavity, may by dilatation lead to the formation of a large cyst. Ferguson, of Albany, has observed one of more than a liter capacity.

The *postanal gut* may in like manner lead to the formation of cysts in the pelvis.

The *ducts of Müller* occasionally remain in postnatal life, and by cystic distention form the so-called *hydatids of Morgagni*, which are so frequently observed attached to the fimbriæ of the Fallopian tube.

Gärtner's ducts also sometimes fail to disappear, and by cystic dilatation form the cysts of the paroöphoron.

9. **Hermaphroditism.**—Although the majority of cases of supposed hermaphroditism might be included among the schistoses and synactoses, there are certain rare cases in which the defective development is more radical and important, so that it is well to have a special heading under which to discuss them.

Hermaphroditism may be true or false.

I. **True hermaphroditism** (androgynes) is characterized by the occurrence of the essential sexual organs both of male and female in the same individual.

Klebs describes three possible forms in which this condition can occur:

1. *Hermaphroditismus verus bilateralis*, in which both ovaries and testes can be present upon both sides, or in which an organ compounded both of

ovarian and testicular tissue may be present on each side. Excepting one case reported by Heppner, no such condition has been observed in man.

2. *Hermaphroditismus verus unilateralis*, in which both sexual glands are present on one side, while that proper for the individual is present on the other side of the body. No authentic case has been observed.

3. *Hermaphroditismus verus lateralis*, in which an ovary is present on one side and a testis on the other side. This condition is very rare, but numerous cases have been reported. Unfortunately, in most cases the final proof of a microscopic examination, with demonstration of ovarian and testicular structures, is wanting.

II. **Spurious hermaphroditism** or *pseudohermaphroditism* is common, nearly all reported cases being properly so classified. These cases usually depend upon malformation of the external genital organs that makes difficult or impossible the recognition of the true sex during life, though dissection reveals the glands of one sex only, and at once explains the true nature of the case.

The cases are separable into: (*a*) Pseudohermaphroditismus masculinus; (*b*) Pseudohermaphroditismus femininus.

(*a*) *Pseudohermaphroditismus masculinus.*

1. *Pseudohermaphroditismus masculinus externus* is characterized by a departure of the male external organs from their normal type and an approximation to the female type. The deformity usually depends upon hypospadias and cleft scrotum with hypoplasia of the penis. The diminutive penis being separated and presenting the urethral orifice deeply seated somewhat resembles an atypical development of the clitoris and nymphæ, while the fissure of the scrotum simulates the vaginal orifice, and its lateral halves the labia majora. The resemblance of the cleft scrotum to the labia majora is greatly increased in cases of undescending testicles. For many reasons not yet understood, in this malformation of the male organs the general body development is frequently atypical and approximates the feminine type, with small stature, rounded curves, and enlargement of the mammæ. Hair may or may not grow upon the face, and the voice may be high-pitched or sonorous.

2. *Pseudohermaphroditismus Masculinus Internus.*—With or without considerable malformation of the external organs, these cases are characterized by the presence of rudimentary female internal organs. At the colliculus seminalis the prostate gland is pierced by a tubular structure which is the homologue of the vagina, and is sometimes readily recognizable as such by its connection above with a uterus and Fallopian tubes. No ovaries are present.

3. *Pseudohermaphroditismus masculinus internus et externus*, in which, with pronounced feminine appearance of the external organs, vagina, uterus, and Fallopian tubes are present, but neither testicles nor ovaries occur.

(*b*) *Pseudohermaphroditismus femininus.*

1. *Pseudohermaphroditismus femininus externus* is characterized by an enlargement of the clitoris and constriction of the vaginal orifice that give the external organs a remarkable resemblance to the masculine type. The penis-like clitoris is not penetrated by the urethral canal.

2. *Pseudohermaphroditismus femininus internus* is produced by the presence in the broad ligaments or in the ureterovaginal walls of rudiments of the Wolffian ducts, and sometimes extending to the clitoris.

3. *Pseudohermaphroditismus femininus externus et internus*, in which the external genital organs resemble those of the male, while the persistence of parts of the Wolffian ducts, and in some cases the presence of a prostate gland, an ejaculatory duct, and a sac resembling a seminal vesicle opening

into the vagina, have also been observed. This form of malformation is rare, but few cases having been observed.

As in *pseudohermaphroditismus masculinus*, so in these forms the development of the whole body departs from the normal type, women often developing to masculine proportions and having a growth of hair on the face. Cases are on record which have lived and died without the true sex having been established and having always supposed themselves to be men.

The body development in cases of pseudohermaphroditism is a matter of peculiar interest, inasmuch as it is supposed that its regulation is governed, at least in part, by an internal secretion of the sex glands. Why a male pseudohermaphrodite with testicular tissue should approach the female type of structure, and a female pseudohermaphrodite with ovaries the male type, is at present unexplained, though it might be conceded that the correspondence is never perfect, and the failure of such individuals to perfectly conform to either type might depend upon absence of the internal secretions of both sets of glands.

Double Malformations; Double Monsters (Monstra Duplicia).—These extraordinary freaks of nature depend upon duplication of the whole body, the halves remaining attached to one another, or to duplication at the cephalic end or at the caudal end. The duplication may be equal or unequal.

The double monsters always arise from a single ovum, and are always of the same sex. The accident that governs their formation takes place at the earliest period of development, probably at the time of the formation of the primitive streak and medullary groove.

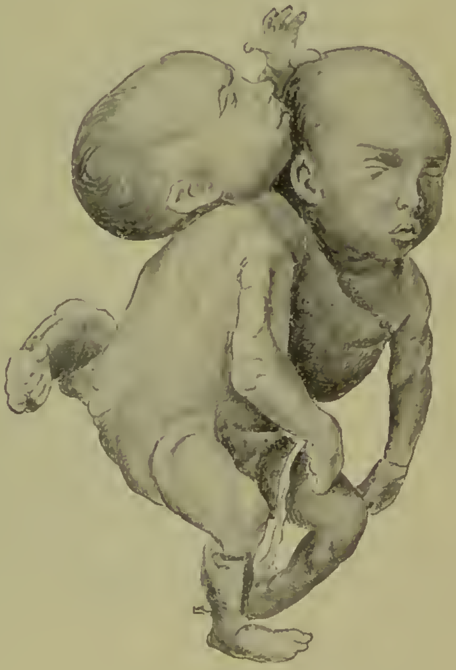

FIG. 16.—Thoracopagus (Ziegler).

Tracing the formation of the embryo from the fecundated ovum through the mulberry and blastula stage, we find the first appearance of embryonal development a circular white area which Kölliker first pointed out. This spot is the embryonal area, and over it the ectoderm of the bilaminar blastodermic vesicle becomes thickened by enlargement of the cells, so that it becomes thickened and pyriform in shape. Later, becoming elongate and having its posterior extremity drawn out into a wedge-shaped appendage, this becomes the "primitive streak," and it is there that the mesoblast spreads itself out over the whole embryonic area between the ectoderm and entoderm. The medullary groove forms in front of this primitive streak, and the embryonic area becomes differentiated into the paraxial portion which is about the groove, and the outer lateral portion. The development of the body is by successive development of these two portions.

Ziegler gives the following theories that may account for the occurrence of double monsters:

1. Two embryonic areas may arise in the wall of a single blastodermic vesicle, grow, and impinge upon one another.

2. Within a single embryonic area two primitive streaks and two medullary growths may form, remaining separate or merging.

3. A primitive streak may form but the medullary groove be double, either in a part or the whole of its extent.

4. A duplication may take place at a later period of development, affecting only individual parts.

The experimental evidence thus far collected indicates that the formation of several embryonic areas does not depend upon fertilization by several spermatozoa, as was once supposed, because eggs thus fertilized always die. It also shows that double formations can arise from supposedly normal eggs by experimental external influences, and that embryonal elements brought into contact may merge one into the other.

The classification of double monsters given by Ziegler seems to afford an excellent working-basis for the understanding and differentiation of nearly all cases, and to it close adherence is given in the following descriptions:

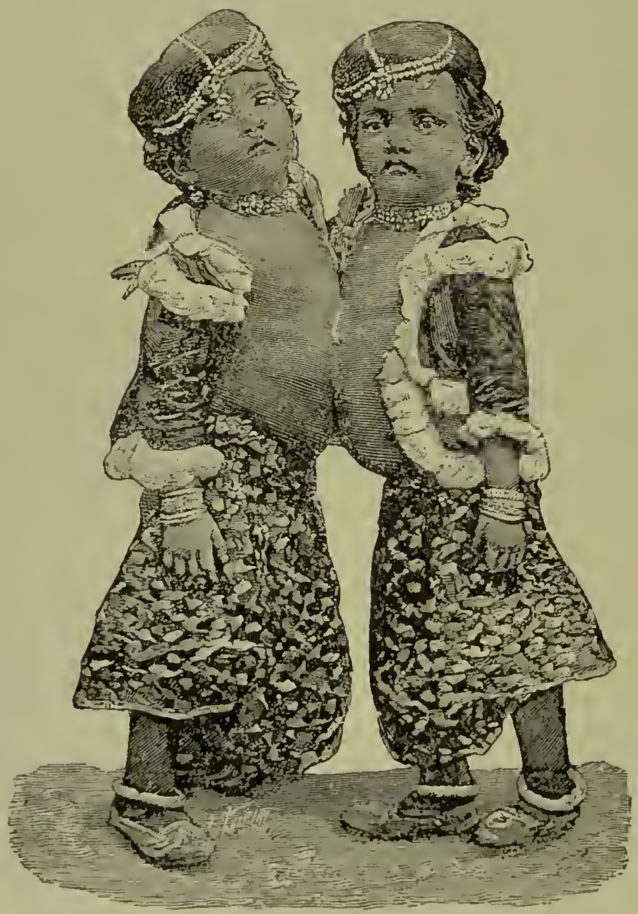

FIG. 17.—Xiphopagi.

I. Double Malformations in which there is Complete Duplication of the Axial Structure.

1. *Characterized by uniform development of both twins.*

(*a*) *Homologous twins* result when development progresses unhindered. They are always of the same sex; each forms its own amnion; they have a common placenta in almost all cases.

(*b*) *Thoracopagous Monsters; Omphalopagous Monsters.*—These forms are caused by coalescence of the trunks of the fetuses. They usually have a common umbilicus and umbilical cord and a single placenta. According to the extent and position of the coalescence they are divided into:

Xiphopagi—united only at the xiphoid cartilage by a bridge of cartilaginous tissue (Fig. 17). Through the band of union there may be a communication between the peritoneal cavities, and contiguous viscera may be united. The "Siamese twins" belonged to this group.

Sternopagi have a common thorax. There are varying degrees of coalescence and deformity. There may be one sternum or two. Sometimes there is but one heart. The intestine may be common to both. The livers may be united.

When thoracopagous monsters are more intimately blended, the union may extend both over the thorax and abdomen, and the limbs and even the heads may be partly fused. Thus:

Prosopothoracopagus—face and thorax coalescent (Fig. 18).

Cephalothoracopagus—head and thorax coalescent.

Thoracopagus tribranchius—thorax and two arms fused so that the monster has three arms.

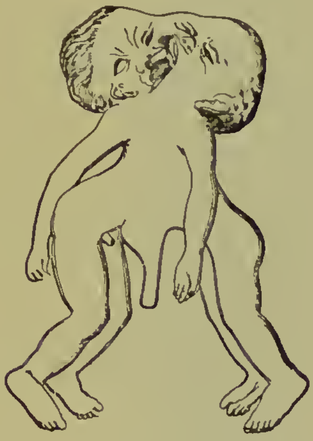

FIG. 18.—Prosopothoracopagus.

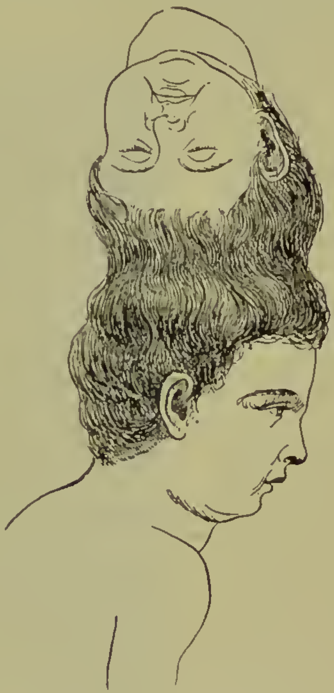

FIG. 19.—Two-headed boy (Home's case).

Thoracopagus tripus—thorax, abdomen, and two legs coalescent, the monster having three legs.

Thoracopagus tribranchius tripus—thorax, abdomen, two arms, and two legs coalescent, the bodies being fused and the monster having three arms and three legs. In these cases of fused extremities the fusion often expresses itself by the presence of misshapen limbs with extra fingers and toes.

Thoracopagous monsters may or may not be viable, according to the deformity of the internal organs. The Siamese twins and Radica-Doddica, or the Orissa sisters, were famous exhibitionists and attained adult life.

(*c*) *Craniopagous monsters* are attached to one another by cartilaginous or osseous unions of the cranium; they are rare. The unions have been observed at the forehead, occiput, and vertex (Fig. 19). Cases have been known to live for many years.

(*d*) *Ischiopagous monsters* are united by the pelvis. This condition is not at all incompatible with life, and numerous cases occur in the literature, of which the "Biddenden Maids," the "Hungarian Sisters," the "Blazek Sisters," and "Millie-Christine" (Fig. 20) are quite famous.

2. *Characterized by unequal development of both twins.*

Some of the most interesting and most peculiar monstrosities are formed through the cessation of growth of the one and progressive growth of the other. When one of twins is deprived of nourishment from any cause, it may die without modification of form or may undergo interesting changes. At times, however, its fellow may assume its nutrition. When this is the case the *autosite*, or well-nourished fetus, may grow normally or may more or less enclose its fellow, of which it makes a *parasite*.

(*a*) *Fœtus Papyraceus.*—This is a dead fetus which, through the pressure of its living twin and absorption of its amniotic fluid, becomes flattened out and thinned. The death of such fetuses is usually referable to too intimate relationship between the umbilical vessels of the common placenta.

(*b*) *Acardiacus.*—Monsters without hearts are always extremely atypical in structure, and, of course, never viable. An acardiac monster may be connected only to the placenta, or may be parasitically attached to its twin.

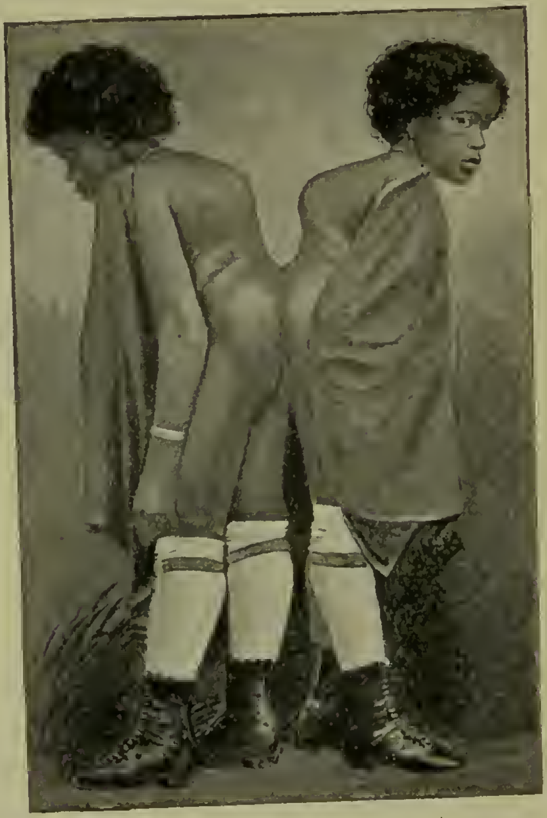

FIG. 20.—Ischiopagi (Pancoast).

Three forms of acardia are described:

Acardiacus amorphus—an irregular mass covered with skin and containing only rudiments of organs.

Acardiacus acormus—the head developed, but the entire body wanting.

Acardiacus acephalus—without a head, the thorax rudimentary, the pelvis and adnexa more or less well developed. It is the most frequent form.

(*c*) *Thoracopagus parasiticus* is seen in thoracopagous twins when the one, from any cause, ceases to develop and remains as a parasitic appendage of the other. Very rarely does such a parasite exhibit complete structure, and in most cases it is an *acardiacus acephalus* or *acormus* with a vascular system blended with that of the autosite.

(*d*) *Epignathus.*—This is a *prosopothoracopagus* which is parasitic at the mouth of its twin, projecting as an imperfectly formed fetal mass. In rare cases it may spring from the orbit.

(*e*) *Teratomata.*—A teratoma is a tumor of such complicated structure as to suggest that it originates either through the dwarfing, malformation, and inclusion of a twin, or a very atypical and erratic development of a single fetus.

The structure of such a tumor usually presents tissues representing all three layers of the blastoderm, sometimes with, sometimes without, definite arrangement. In some cases rudiments of skeletal parts, with recognizable fragments of spinal columns and pelves, are present. In the ovarian dermoid tumors, which belong to this class, bones, teeth, hair, mammary glands, tubular diverticula resembling atypical digestive organs, etc., are present. It is a question how the ovarian dermoids develop, but they are certainly teratomata, whether the result of parthenogenesis, as suggested by Wilms, or of fetal inclusion.

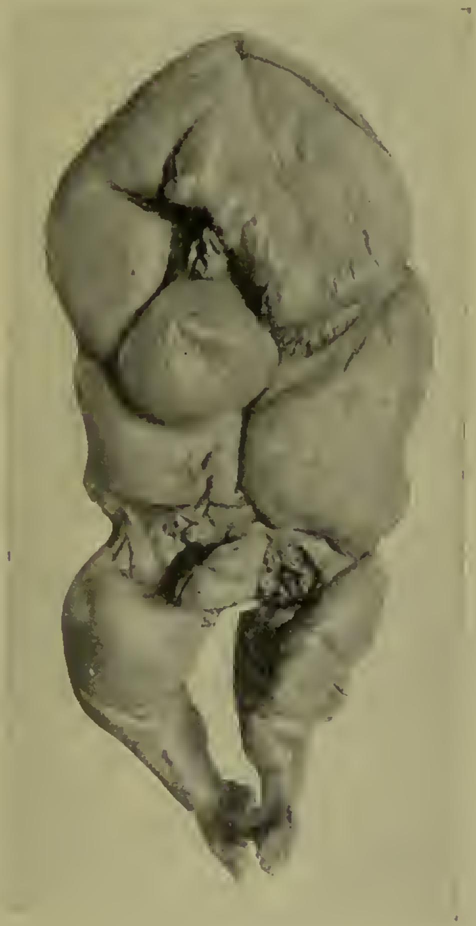

FIG. 21.—Acephalus acardiacus dipus (Lewis).

Teratoid tumors are most frequent about the pelvis, and are frequently styled sacral teratomata. If the tumor is sufficiently formed to resemble an attached fetus, it is known as an *epipygus*.

(*f*) *Inclusio fœtalis* is the explanation of some of the teratoid tumors and for other deeply seated embryonal masses. Inclosed fetuses are probably very rare, unless the ovarian dermoids are so regarded. They are classified according to the seat of occurrence as *inclusio abdominalis, mediastinalis, subcutanea, cerebralis, testiculi, ovarii*, etc. Inclusion affords a satisfactory explanation for the occurrence of many very obscure tumor formations.

II. **Double Malformations in which there is an Incomplete Duplication of the Axial Structures.**

These conditions result from anterior or posterior splitting or duplication of the primitive embryonal area and medullary groove. If such cleavage takes place at the anterior end, it results in a two-headed monster, or one with two heads and several arms, with incomplete division of the thorax and a single pelvis and one pair of limbs.

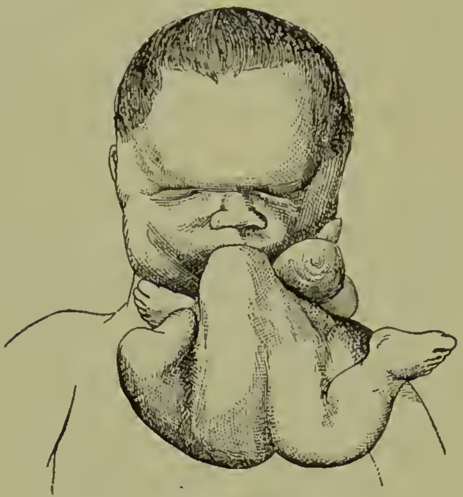

FIG. 22.—Epignathus.

If, on the other hand, the cleavage is posterior, there may be four legs, a double pelvis and imperfectly divided thorax, with a single pair of arms and one head.

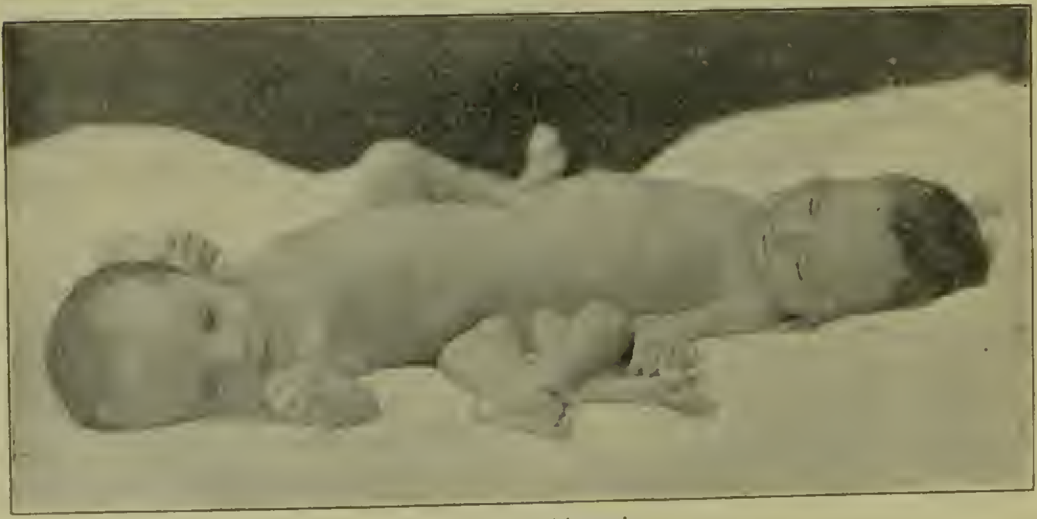

FIG. 23.—Ischiopagi.

The resulting malformed individuals may or may not be viable, those in which the anterior end is affected frequently having an entanglement of nervous systems precluding successful physiologic action. Cases of posterior division, except the abdominal organs are too imperfect, usually are viable.

It is plausible to think that the coalescence that has been shown to be a factor of importance in the union between twins with complete duplication of the axial structure may also play an important part in the present variety of deformity, causing coalescence of parts that may have been quite well differentiated originally. As in the monsters of the other class, the parts may develop symmetrically or may outgrow one another.

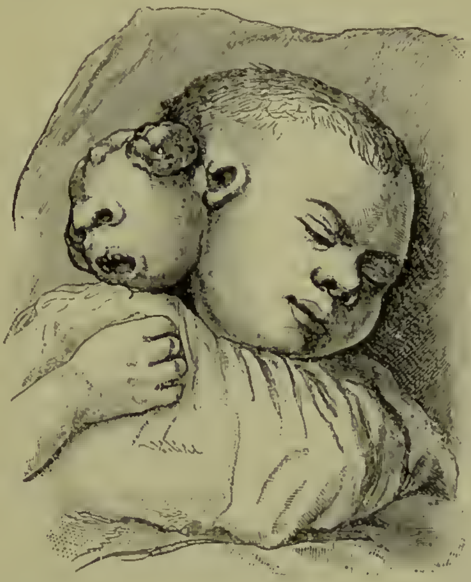

FIG. 24.—Infant with a supernumerary head (after Sutton).

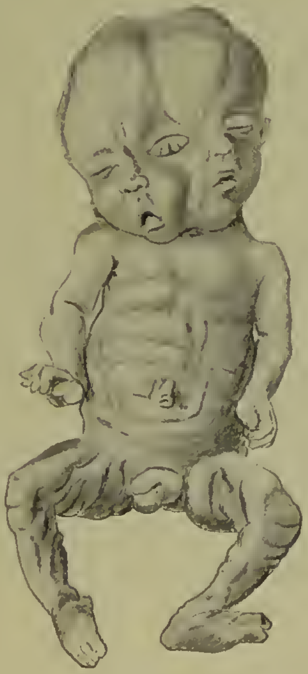

FIG. 25.—Diprosopus (Ziegler).

1. *Duplicitas Anterior, or Terata Catadidyma Anterior.*—The duplications

are more frequent at the anterior end of the embryo than at the posterior. The most frequent form is that in which a double face occurs. It is known as *diprosopus* (Fig. 25), and accordingly, as with the double face, there are two mouths, two, three, or four eyes, two or four ears; the different forms are subdivided into *distomus*, *diophthalmus*, *triophthalmus*, *tetrophthalmus*, *diotus*, etc.

When the division extends so deeply that two distinct heads occur, the chances of viability are increased. The monster is known as *dicephalus* (Fig. 26), and may have two, three, or four arms (*dibranchius*, *tribranchius*, *tetrabranchius*). Cases with the cleavage of the body descending so low that there are four arms usually have two hearts.

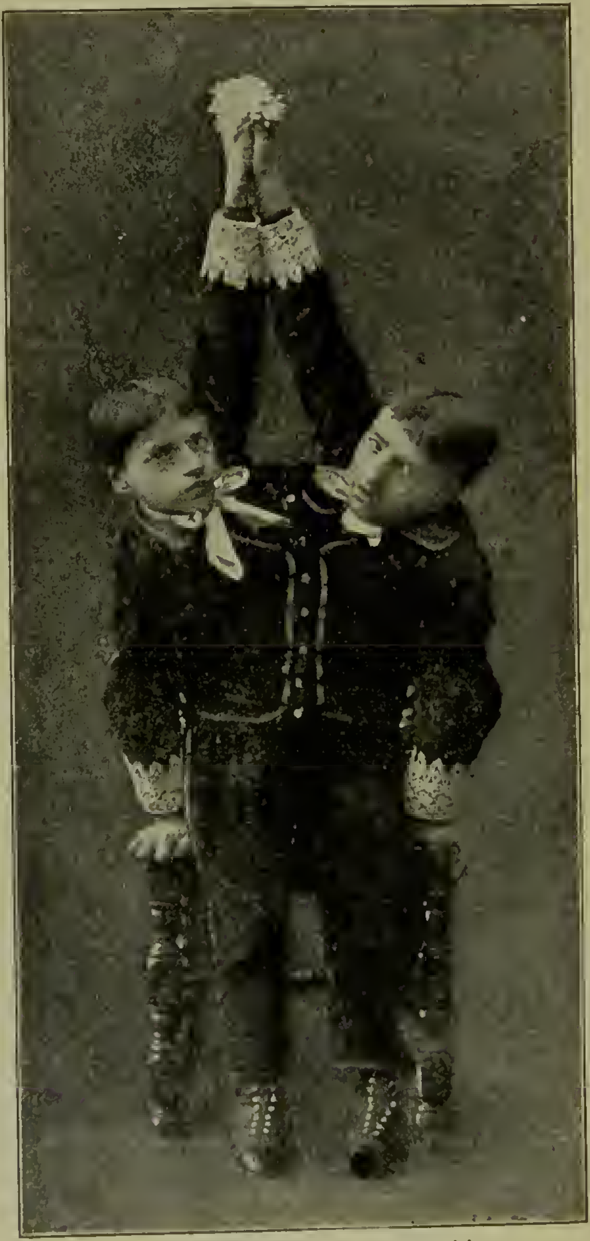

FIG. 26.—Dicephalus tetrabranchius.

Sometimes one of the heads of the dicephalic monsters remains rudimentary and appears as a parasite upon the other (Fig. 24).

When the division of the bodies descends to the pelvis, so that there are two complete vertebral columns but only one sacrum and coccyx, the monster is called *pygopagus*.

2. *Duplicitas posterior* is rare in man, and is nearly always quite imperfect. In extremely rare cases there have been four legs, two sets of genital and pelvic organs, with single development above.

The duplication in most cases involves an atypical development of the supernumerary limbs. It is quite usual for one set of limbs to develop normally, while the other set is deformed and often quite small. The malformed limbs are also apt to be abnormally attached.

The posterior cleavage may extend higher up than the pelvis and cause a duplication of the whole spinal column and part of the head. In these cases the twins usually face one another, and while the backs may be quite well formed, the abdomens, thoraces, and faces may be common (*prosopothoraco-omphalopagus*). The *syncephalus* which occurs in such cases may afford what is known as the Janus head, with two lateral faces with imperfectly differentiated eyes, mouth, nose, etc., and confusion of cranial and cerebral structure. These cases are not viable.

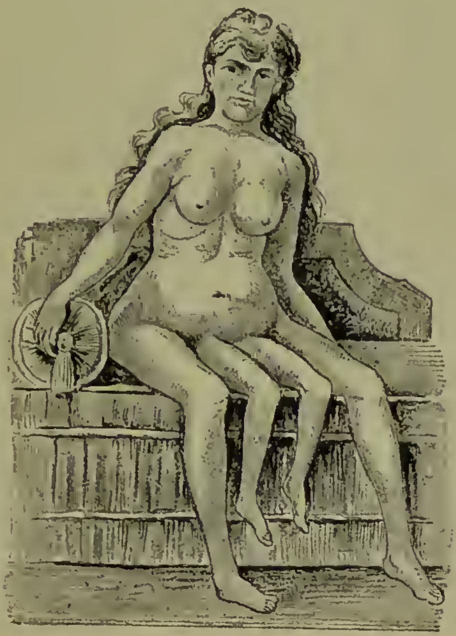

FIG. 27.—Dipygus (Wells).

When complete duplication of the bodies is associated with a single head, the condition is described as *dipygus*. The two portions usually fail to develop symmetrically, so that in nearly all cases the one half remains dwarfed or rudimentary and is a parasite upon the other (*dipygus parasiticus*). Laloo, the Hindoo monstrosity (Fig. 28), is an illustration of this form.

In dipygus parasiticus the parasitic portion is more highly developed in those cases in which it springs from some point near the head of the autosite than when it arises lower down. If it arise from the neck of the autosite, it may have a trunk and all four limbs; if from the spinal column low down, only lower extremities.

3. *Duplicitas parallela* or *rachipagus* is a form of monstrosity supposed to be occasioned by partial cleavage from each end, so that the twins are only

attached at some circumscribed part of the spinal column. Unless it could be shown that the spinal column was double to a certain point, then became single to become double again lower down, it would seem more logical to regard such cases as *thoracopagi*—that is, *rachipagus*.

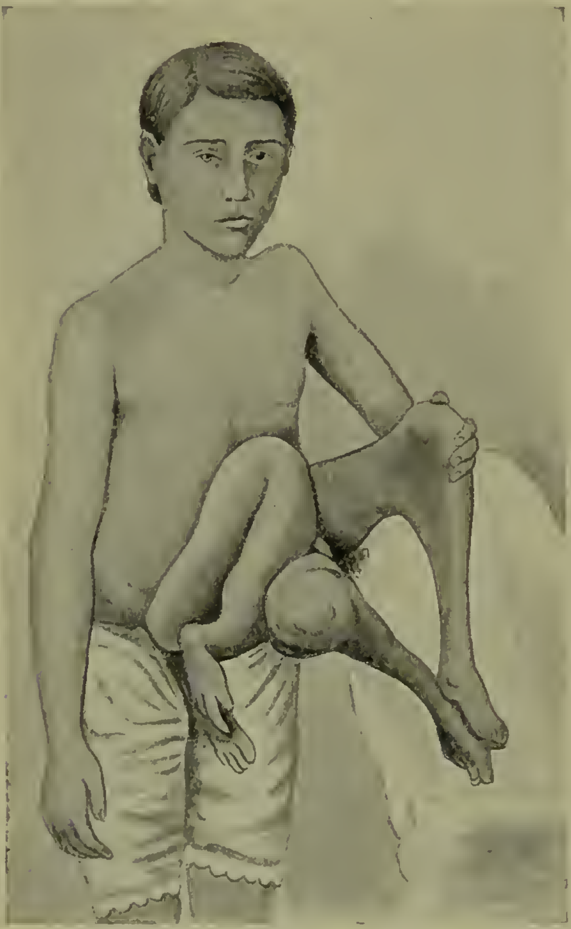

FIG. 28.—Laloo, a Hindoo with an acardiac parasite attached to the thorax.

The physiology of the duplicate monsters is very interesting, especially as it concerns the nervous system. There is, however, no regularity about it, each case being more or less a law unto itself.

Triple monsters and *multiple monsters* have occurred, and some authentic cases are recorded with descriptions. Their mode of origin and general peculiarities correspond with the double monsters.

CHAPTER III.

PATHOLOGY OF NUTRITION.

THE molecular structure of living matter is unstable and ever changing. It is continually subject to "universal disintegration and waste by oxidation; and concomitant reintegration by the intussusception of new matter." It is by the intussusception of new matter that living beings are enabled to manifest uninterrupted activities throughout long periods of time. Through it alone is possible that extraordinary ability to grow and multiply that differentiates inert matter from the vital world.

Continuance of life, activity, growth, and reproduction are all indissolubly bound up in the intussusception of new matter into the cytoplasm of the cells. The ovum grows and divides, but almost immediately calls upon its reserve supply of food for the successful progress of its development. Large reserve supplies, such as are seen in the eggs of birds, suffice to carry the chicks to a stage when they can begin, with or without the help of parents, to secure and utilize new and extrinsic food supplies, out of which they must manufacture their own nutrient tissue pabulum. The cells of the growing body and the active cells of the adult body require constant supplies of assimilable materials from which to increase their cytoplasm, form nuclein, abstract secretions, and build up their various products.

The new matter appropriate for cellular reintegration is called *food.* The utilization of food constitutes *nutrition.*

A food, therefore, is any material contributing to the formation and reintegration of the tissues. The form in which foods present themselves varies greatly. Certain of the lowest vegetable forms of life can, in the presence of moisture and certain gases diffused through the atmosphere, synthetize all that is essential to life. Higher plants require additional chemical elements, and are best fed with nitrogenous "fertilizers." Low forms of animal life absorb invisible nourishment from the water in which they live; the entozoa absorb highly nutritious, diffusible juices from the intestines of the animals they infest. Many lowly organized animals take minute objects into their substance and digest and assimilate them; the higher animals find their food in already-formed vegetable tissue, or in the tissues of other animals.

Water is one of the most important foods, and without it no other food can be utilized, as it is essential that the nutritious substance find itself in a form easily assimilable and readily conveyed to the cells. To accomplish these requirements, all animals and plants reduce the nutrient substances to soluble forms, dissolve them in water, and then distribute the solution to all their parts, either by cytoplasmic currents, flow of sap, or circulation of blood.

The *necessity for food* varies according to the activity of the individual. Serpents consume large quantities of food at a single gorge, but do so at very infrequent intervals, and it is not uncommon to find captive serpents fasting during periods varying from a few months to a year and a half. The more active animals, as, for example, the birds, are continually seeking for and devouring food. Whether taken frequently or infrequently, in large amounts or small ones, the total quantity of food consumed must be sufficient to reintegrate the oxidized and wasted tissue elements, supply the materials for the various secretions, and provide for growth and reproduction. In order that a normal, average, adult man is able to do this and perform ordinary work, the studies of Moleschatt, Ranke, Voit, Forster, and Atwater show that he requires about 635 gm. of solid food every twenty-four hours. This food is made up of proteids, 123 gm.; fats, 78 gm., and carbohydrates, 437 gm. The amount of water required is between 2000 and 3000 gm. Certain salts are also indispensable in the physical processes of the body chemistry. The total quantity required is unknown, probably about 50 to 75 gm., and, as they are usually consumed together with the foodstuffs, they need no separate mention.

Under normal conditions the *appetite* is a satisfactory guide concerning the food consumption. In disease, however, it may so vary as to be entirely untrustworthy. There is, for example, a condition known as *bulimia*, in which the appetite is enormously exaggerated, and an opposite condition known as *anorexia*, in which it is greatly diminished or even absent. Perverted appetite, or *pica*, also occurs in all grades, from an excessive desire for candy or pickles to the disgusting extreme of cannibalism or earth-eating. Actual fear or dread of food is described as "*sitophobia*."

Thirst may also vary from the normal, marked increase being known as *dipsesis* or *polydipsia*, which is a prominent symptom of diabetes mellitus, and in which the thirst may be so insatiable that, when other fluids have been withheld, patients have been known to drink their own urine. Perverted thirst has its most common and unfortunate occurrence in *dipsomania*, or excessive desire for spirituous liquors.

Swallowing air by spasmodic efforts has been called *aërophagia*.

When food is withheld and the wear and tear of the tissues is not compensated for they gradually waste by oxidation, beginning with those least useful, as the adipose tissues, next extending to the muscles, and finally involving those important tissues upon the performance of whose functions life depends. This condition is known as *starvation*, and will be further discussed under the heading Assimilation of Food.

Excess of food is usually far less serious than starvation, though it is not without its dangers. Individuals vary greatly in their abilities to digest and utilize foods. Savage peoples, with whom periods of plenty alternate with periods of starvation, make a practice of gorging themselves with food until they fall into a satisfied sleep. Should ordinary civilized people overload their stomachs in such manner, there is little doubt but that the muscular structure of the stomach would resent the unusual distention and relieve itself by the process of *vomiting*. Should this not occur, the food would probably be hurried partially digested into the intestine, where it would likely set up an *irritative diarrhea* (*crapulous* or *lienteric diarrhea*). Should the consumed food be digested and assimilated, the inevitable outcome is the addition to the tissues of an excess of nutriment that is usually stored up as fat.

Continuous hypernutrition with accumulation of adipose tissue ultimately leads to *obesity*, and in extremely pronounced cases to *polysarcia*.

The water consumed by the individual is more easily disposed of than the food, and usually meets with a rapid elimination by the kidneys as urine, producing temporary *polyuria* or *diuresis*, or by the sweat glands as *perspiration* (*diaphoresis*).

PATHOLOGY OF DIGESTION.

An analysis of the required foodstuffs shows that they fall into three chemical groups—*proteids*, *carbohydrates*, and *fats*. Each of these has its own digestive enzymes, which it meets at some particular part of the alimentary apparatus, and undergoes its own peculiar changes.

(*a*) **Digestion of Proteids.**—*Albumins and Albuminoids.*—Proteid digestion takes place partly in the stomach and partly in the small intestine through the agency of pepsin and trypsin, two active ferments, the former of which is secreted by the gastric glands, the latter by the pancreas. The effect of both ferments is the transformation of the non-diffusible albumins to diffusible peptones. Pepsin is active only in strongly acid solution; trypsin in alkaline solution. The chemical changes resulting from the action of the ferments upon albuminous substances are similar though not identical. In *peptic digestion* the first change resulting from the action of the hydrochloric acid and pepsin of the gastric juice upon the proteid is its conversion to an acid albumin or *syntonin*. From this it is next converted to *primary albumose* or *primary globulose*, then to secondary or *deutero-albumose* or *proteose*, and finally to diffusible *amphopeptone*. Beyond this stage of amphopeptone the peptic digestion does not progress.

In *tryptic digestion* the steps of the process as well as its termination vary somewhat. The proteids are at once converted to *deutero-albumose* or *globulose*, then to *amphopeptone*, but the process does not end there, as the amphopeptone is converted partly into *antipeptone* and partly into *hemipeptone*. The antipeptone is diffusible and useful; but the hemipeptone is subject to further conversions until such end-products as leucin, tyrosin, aspartic acid, tryptophan, and various acids, bases, and aromatics are formed.

Trypsin also acts more actively upon albuminoids than does pepsin. Gelatin is converted to gelatose by pepsin, but to gelatin-peptone by trypsin.

Pathology of Proteid Digestion.—*Peptic digestion* takes place only in the stomach. As pepsin is active only in the presence of free hydrochloric acid, its operation upon the proteids ceases as soon as the chyme is poured into the intestine and meets with its alkaline juices.

Peptic digestion may be retarded or modified by

(1) Abnormal secretion of pepsin. (2) Abnormal quantity of free acid.

It seems rarely to happen that the pepsin itself is secreted in amounts insufficient to carry on the function of digestion, but there are cases of atrophy of the stomach and chronic interstitial gastritis with destruction of the peptic glands in which this may happen.

Much more commonly the hydrochloric acid is at fault. In the great majority of cases of carcinoma ventriculi, especially of pyloric carcinoma, no free hydrochloric acid is secreted (*achlorhydria*). In many neurasthenic and anemic individuals the quantity of hydrochloric acid is markedly reduced (*hypochlorhydria*). In less frequent cases the acid is present in excess (*hyperchlorhydria*).

Remembering that the trypsin of the pancreatic secretion is much more powerful in its action upon proteids than the pepsin, it might be inferred that the interruption of gastric digestion is of comparatively little consequence, especially as animals can live after experimental removal of the stomach. We find in practice, however, that no aberration of the gastric function can take place without the occurrence of disagreeble symptoms, and no suspension of those functions without serious and somewhat fatal results.

In conditions in which there is a deficiency of pepsin or of hydrochloric acid the food is retained for an abnormally long time in the stomach, distending it, undergoing putrefactive changes, and either stimulating the organ to reject it by vomiting, or passing it on in an unprepared condition to the intestine, which bears the burden of excessive work. In the beginning the individual bears this fairly well; but in the course of time emaciation, anemia, and other changes present themselves as evidences of malnutrition.

In cases of achlorhydria associated with pyloric obstruction two additional evils are encountered: first, the suspension of digestion, which permits ready decomposition of food in the stomach and leads to the formation of irritating and partially poisonous substances, that are in part vomited, in part absorbed, and the inability of the food to enter the intestine, where it might be digested. In such conditions as these, too much importance must not be attributed to the chemical abnormalities only.

The opposite condition, in which too much hydrochloric acid is present in the gastric juice, is seen in Rossbach's disease, or *hyperchlorhydria* or *gastroxia*. Here the excessive acidity leads to eructations of acid fluid, vomiting of acid materials, headache, and general distress. This condition is probably a neurosis, but interferes with nutrition by exciting the stomach to reject the food and by depressing the general body condition.

The corrosion of the gastric wall by its contents is a matter of much interest, and will be discussed at some length under Diseases of the Stomach. So long as the gastric tissues retain their vitality, they are immune against the action of their own secretion; but as soon as any part of them becomes necrotic, it is at once attacked and digested. It is in this manner that the *peptic ulcers* are formed. After death the gastric juice at once begins to attack the tissue, causing the postmortem softening described as *gastromalacia*.

(*b*) The **digestion of carbohydrates** takes place in the mouth and in the stomach through the agency of *ptyalin*, a ferment of the saliva, and in the intestine through the action of *amylopsin*, a ferment of the pancreatic juice. Foods remain in the mouth so short a time that the action of ptyalin upon them is of short duration and must be productive of very limited result. Ptyalin digestion continues in the stomach for a short time, but as soon as .003 per cent. of free hydrochloric acid is present it ceases. Lusk has found that cane sugar can be inverted to dextrose and levulose in the stomach, but a study of the gastric juice, of proteid digestion, and of the gastric contents during digestion, convinces one that the stomach is intended for the digestion of proteid substances only.

It is in the intestine, therefore, through the activity of the pancreatic enzyme amylopsin, that the digestion of carbohydrates is accomplished. In passing it may be well to remark that the ptyalin and amylopsin digestions in no way differ from one another, and that the enzymes are identical so far as can be determined. The *succus entericus* also contains an amylolytic enzyme of its own. Ptyalin and amylopsin act upon starches, converting them to sugar, the end-product of this conversion being maltose. The conversion is not a direct one, the complexity of the starch molecule probably preventing this. The process seems to take place through the assumption of water by the starch, with the formation of soluble starch or *amylodextrin*. The molecule then splits, with the formation of maltose and a form of dextrin which, because of the red color that it strikes with iodin, is called *erythrodextrin*. The same hydrolytic process now repeats itself with the formation of more maltose and another form of dextrin, the *achroödextrin*, which becomes *maltodextrin*, and finally *maltose*.

The final step in ptyalin and amylopsin digestion is thus seen to be maltose; but there is a further transformation of carbohydrates brought about by the activity of an inverting ferment (*invertin*) secreted by the intestinal epithelium, by which the maltose is transformed to dextrose, in which form it is absorbed.

Pathology of Carbohydrate Digestion.—The rarity of recognized serious disease of the pancreas, and the occurrence of an amylolytic ferment in the intestinal secretion, combine to make it difficult to determine the cause of the pathologic changes of carbohydrate digestion. There seem to be few conditions in which failure of carbohydrate digestion becomes important or serious.

However, fermentative changes produced by the intestinal bacteria may lead to irritative diarrhea.

(*c*) **Digestion of Fats.**—Fats are digested through the agency of an enzyme of the pancreatic secretion (*steapsin*) and by the bile. Our knowledge of the process is limited. In all probability the fat is acted upon by the steapsin and split by hydrolytic cleavage into glycerin and fatty acids. The fatty acids combine with the alkaline salts of the bile and intestinal juices, forming soaps. The glycerin and soaps are readily diffusible, and it is in these forms that the fats are absorbed.

Pathology of the Digestion of Fats.—The activity of the oleolytic enzyme (steapsin) is sometimes observed in disease or injury of the pancreas, in which some of the secretion escapes into the surrounding cellular and fatty tissues. Under these circumstances, rounded whitish nodules, varying in size from that of a pin-head to that of a hen's egg, of a soft, waxy consistency, and not infrequently infiltrated with lime, are found in the fatty tissue. Their formation depends upon the activity of the pancreatic enzyme, and the condition is usually described as *fat necrosis.*

The presence of fatty matter in the stools is characteristic of pancreatic disease.

The most interesting interference with the digestion of fats is seen in obstructive diseases of the biliary ducts associated with retention of the hepatic, and probably also of the pancreatic, secretions, and associated with the condition clinically known as *jaundice* (*q. v.*). Under these conditions the failure of bile to enter the intestine deprives the contents of their normal coloring-matter, so that the feces become abnormally pale-clay colored. The absence of bile also interferes with the saponification of fats, which pass out in the feces, giving them a pasty consistency.

(*d*) **Water** enters the body both as a component of the softer foods and as a beverage. It requires no digestion or transformation.

(*e*) **Inorganic salts** of various kinds are indispensable to many of the vital processes. They are consumed, for the most part without our knowledge, as constituents of other foodstuffs. Sodium chlorid, which is of special importance, is, however, especially sought out and consumed in quantities beyond the actual need, as is evinced by its elimination in the urine. Potassium, calcium, and magnesium salts are components of important tissues; iron is one of the important elements of the hemoglobin molecule; phosphorus and sulphur in various combinations are of importance.

The inorganic salts are probably of more importance in facilitating osmosis and exosmosis, stimulating secretion, bringing about certain important syntheses and analyses, than in simply entering into the composition of the tissues.

ASSIMILATION OF FOOD.

The assimilation of the digested foods depends upon vital cellular energies, the nature of which is still undetermined. The digested proteid substances are reduced to transfusible albumoses, and presumably pass from the intestine, in which the transformation is completed, into the capillary blood as it circulates in their walls. It is, however, changed as it passes from the intestine to the blood, for, while we find the peptones and albumoses in the intestine, we find neither in the blood, the passage through the cells serving to transform the diffusible albumoses and peptones again to albumin—the serum albumin of the blood. It is the serum albumin thus formed that circulates in the blood and supplies to the tissues their chief proteid food.

The carbohydrate foods having undergone the requisite hydrolytic changes are ultimately reduced to maltose, inverted to dextrose, and absorbed into the blood in this form. Should all of the dextrose entering the portal capillaries during the absorption of digested food pass directly into the circulation, the quantity of sugar in the systemic blood would increase, to fall again in the intervals of digestion. We find, however, that the liver plays a most important function, by which the entrance of the sugars into the systemic blood is accurately regulated. When the dextrose reaches this viscus some passes directly on with the blood, but the excess is taken up by the hepatic cells, hydrated, and converted into glycogen, in which form it is retained until needed to maintain the proper equilibrium, when it is transformed back to dextrose and discharged into the blood current.

The fats transformed to glycerin, fatty acids, and soaps are absorbed in these forms. A few fat globules taken up by the intestinal epithelial cells and by the leukocytes are passed on toward the centers of the intestinal villi, where they ultimately escape into the lymph spaces, become suspended in the lymph, which then receives the name chyle, and, following the lymphatic circulation, reach the thoracic duct, and finally are poured into the blood of the subclavian vein.

Pathology of Assimilation.—The assimilation of food may be (I) diminished or (II) increased.

I. **Diminished assimilation** may depend upon (1) deficient supply of nutriment; (2) deflection of nutriment from its proper channels.

1. *Deficient supply of food* may depend upon actual deficiency of bulk or upon innutritious quality of the substances consumed. The result is in either case the same, the outcome being *starvation*, *marasmus*, *scurvy*, *rickets*, or *asthenia*.

Starvation or **inanition** occurs when the food supply is withdrawn. In the living body the processes of combustion and oxidation go on whether the fuel comes from without or from within, and as soon as the digestive organs cease to throw into the circulation the usual products, the reserve supply is first called upon, then the consumption of the formed tissue slowly takes place. In all probability the circulating proteids are first consumed, as during the first couple of days during starvation about the usual quantity of nitrogen is excreted. After this the glycogen is quickly consumed, then the fats, and then the muscles. The tissue loss may reach 30 to 50 per cent. of the body weight, the chief losses being in the fat and the voluntary muscles. The vital organs—the heart and central nervous system—retain their integrity longest and suffer the least loss of weight, evidently living at the expense of the other organs and tissues. Such wasting is called *emaciation*.

In cases of absolute withdrawal of food and water from human beings, death follows after a period that varies from seven to thirty days. The duration of life is largely influenced by the amount of available fuel stored in the tissues, so that large, fat persons succumb after a much longer interval than others. Exercise increases combustion, hence hastens the final stages. When the consumption of water is permitted life is prolonged and less discomfort is experienced, as a stomach full of water gives a certain sense of gratification. When the slowly sinking temperature is supported by artificial heat, the fatal termination may be delayed.

The digestive organs slowly empty themselves of fecal matter and become smaller and smaller; the bulk of the liver is lessened and the secretion of bile becomes greatly reduced; excretion by all of the organs is suspended. In many the cells degenerate. There are certain well-marked changes in the blood, the leukocytes falling markedly in number, though the red cells remain normal. Stengel suggests that there is really a marked loss in red cells, but the loss of water makes it appear as if the blood were normal.

As the vital conditions become more and more impaired, the walls of the capillary blood vessels yield to the pressure of the contained blood and extravasations occur into the tissues. Death takes place slowly from gradual wearing out of the vital organs, errors of metabolism, or infection. Starvation may be checked at any time by the administration of food and the resumption of the functions of digestion and assimilation unless the tissues of the digestive organs have passed beyond the point of being able properly to deal with the foods, when death is inevitable.

Marasmus and **cachexia** are terms used to describe a more protracted and gradual failure of nutrition than is seen in starvation.

The term *marasmus* is usually employed to describe the emaciation of improperly nourished infants, usually, though not always, the victims of artificial feeding. It is not always the food that is at fault, however, as many infants, because of inherited syphilis or other constitutional vice, are unable properly to digest or assimilate the most appropriate foods. The wasting in these cases is very gradual and continues for months. Death may result, or at any time the removal of the cause of the trouble may permit a rapid convalescence. During the impoverished condition the nutritive processes go on irregularly, and coexistent rachitis is very frequent. Marantic or marasmic infants present a very characteristic appearance. The body is excessively thin and pale, the skin is wrinkled, the visage drawn, and the expression of the face resembles that of senility.

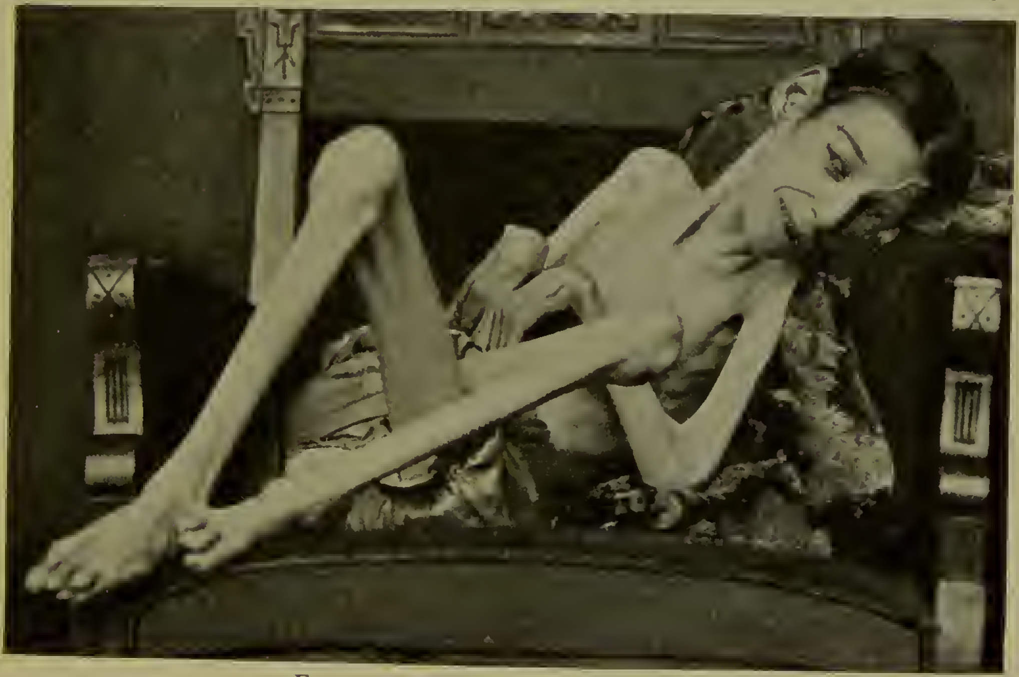

FIG. 29.—Marasmus (Gould and Pyle).

Cachexia is marasmus of the adult, and usually accompanies malignant or other chronic disease. The atrophy of the tissues of the body is slow. There are certain peculiarities of the cachectic state not seen in simple marasmus, among which are a peculiar yellowish color of the skin and a more profound anemia. These suggested to the older writers that the growing neoplasm both abstracted from the blood nutriment for its own tissues, and discharged into the blood deleterious metabolic products which, acting as impurities, so altered the composition of the blood that predisposition to further pathologic changes developed. This condition was described as *dyscrasia.*

Rachitis or **rickets** is a malnutrition of childhood, characterized by structural changes in the bones (see Diseases of the Bones) and in the organs. The nutritive disturbance depends upon other factors than starvation, for when young animals are half-starved for prolonged periods they do not develop rickets. The trouble seems to consist essentially of deficiency of animal foods (proteids) and of certain salts. The chief lesions are situated in the bones, whose articular ends become enlarged through hyperplasia of the epiphyseal cartilages and periosteum. The line of ossification becomes wide and irregular; the formed bone being reabsorbed and deposited in a less regular and more rarefied condition. The new bone is deficient in lime salts, and is, in consequence, more or less plastic, so that the effects of pressure upon the growing bones cause characteristic deformities. There are, usually, associated disorders of the internal organs. Gastro-intestinal disturbances are frequent, and may be primary rather than secondary. The liver and kidneys frequently show fibrous proliferations, suggesting chronic irritation from substances absorbed from the alimentary tract. At one time the disease was thought to depend upon the absorption of lactic acid, but this view of the etiology of the disease has never been substantiated. Occasionally the disease is congenital, and family predisposition seems to occur in many cases. The disease is much more frequent among the poor than among the rich, and among negroes than Caucasians. It is not itself a fatal affection, though large numbers of rachitic children die because of the gastro-intestinal affection, from marasmus, or from infections to which their depraved vital condition predisposes them.

Cases that recover show permanent osseous deformities, of which those of the pelvis are most important because of the difficulty they may cause in parturition.

Scurvy or **scorbutus** is a nutritive disease which, while occasionally observed during childhood, usually appears in adult life. It seems to be the result of unwholesome rather than of insufficient food. Before the days of canned green vegetables, when salt meats formed the chief diet of sailors, scurvy was frequent during prolonged sea voyages. It is rare at present, because salt foods are less used and canned vegetables cheap. The disease depends upon the loss of certain compounds supplied to us only through vegetable foods. Garrod and others believe the condition depends upon an insufficiency of the potassium salts; Rulfe, that it is the absence of citrates, malates, lactates, etc., by which the blood becomes abnormally acid. According to this view, scurvy is a form of acid intoxication.

The disease develops slowly, emaciation and anemia being succeeded by the occurrence of stomatitis. The gums become swollen and spongy, and bleed readily from slight injury; the teeth become sensitive and loosen. Alveolar inflammations occur, probably through infection from the mouth, and the loosened teeth fall out. Sometimes ulcerations form upon the gums, which may become so swollen and fungoid as to obscure the teeth. A marked disposition to hemorrhagic extravasations is observed, and petechiæ, ecchymoses, and suffusions occur in the skin, upon the mucous and serous membranes, and into the muscles and organs. The blood is dark colored and fluid. There are no characteristic morbid lesions visible to the naked eye, and microscopically the only lesions of the organs are interstitial hemorrhages and parenchymatous degenerations.

In cases in which the alveolar inflammations are very severe, necrosis of the maxillary bone has been observed. In severe scurvy of adolescence separations of the epiphyseal cartilages, separation of the costal cartilages from the sternum, and other osseous and chondrous lesions may occur. Predisposition to infection is marked, and wounds fail to heal and fractures to unite.

2. *Deflection of nutriment* with serious consequences is very rare. The digested foods for the most part pass through the capillary wall and are carried in the portal blood to the liver. The great bulk of the assimilated products takes this course. A certain proportion however, is poured into the circulation through the thoracic duct. In the intervals of digestion the fluid passing through the thoracic duct is probably lymph, but during the period of absorption following digestion it contains fat in an emulsified state, and other substances, which impart to it the ability to coagulate readily. When through injury or operation the thoracic duct is permitted to waste its contents through an external fistula, death following progressive emaciation is of frequent occurrence. It would probably occur in all cases were it not for the often present accessory thoracic duct of the right side, the free lymphatic anastomoses, and the recently discovered anastomoses between the lymphatics and veins of the abdomen and thorax. It is difficult to explain why emaciation and death should occur in such cases, as an abundance of assimilable material enters the blood in other ways.

II. **Increased or excessive assimilation** has its dangers in that it leads to the accumulation of certain substances in the body, of which normal amounts are beneficial, but excessive quantities injurious.

Obesity or **polysarcia** is an excessive deposition of fat in the fat-storing tissues. There is little evidence to show that fats can be formed from proteids, but we find that the metabolic processes readily manufacture fats from carbohydrates. Individuals excluding all fats from their dietary continue to take on fat so long as the carbohydrate diet is unrestricted. We can, therefore, suppose that obesity depends upon the formation of fat in the body and its deposition in the tissues. It becomes an interesting question to determine whether the excessive deposition of fat depends upon excessive digestion, assimilation, and transformation of carbohydrates, or whether it depends upon diminished oxidation of these fat-forming elements. Obesity usually occurs in persons naturally possessed of strong digestive powers, who stimulate the digestive function with alcohol and live sedentary, inactive lives. In many cases it accompanies anemia. All of these conditions lead us to assume that both factors are operative, and that though there must be an increased assimilation of carbohydrates in the majority of cases, there is also a deficiency of oxidation by which they are destroyed. Hereditary tendency

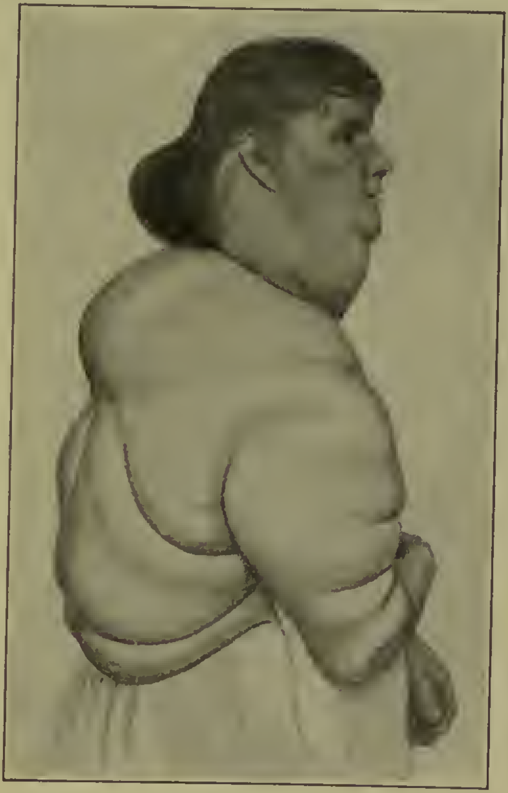

FIG. 30.—Obesity.

to obesity is commonly observed, and probably depends upon inherited active digestive powers or bodily indolence.

It is difficult to define obesity, as there is no distinct limit to the fatty deposits that may occur in health.

The appearances are too well known to require description. The trunk is usually disproportionate to the limbs, though these may be of enormous size. The belly becomes very large and pendulous. Rolls of fat occur about the neck, giving a well-marked double chin, and the mammary glands become very large and pendulous. The weight that may be attained in obesity is almost beyond belief. The most famous of all fat men was probably Daniel Lambert, who at the age of thirty-nine years weighed 616 pounds. Women also may occasionally reach this extreme size; Millie Josephine, of Chicago, at the age of thirteen (?) measured 5 feet 6 inches, and weighed 422 pounds. Children may also suffer from obesity, there being a collection of such cases in Gould and Pyle's "Curiosities and Anomalies of Medicine." Among them is recorded a little girl of four years, who weighed 256 pounds.

Certain parts of the body always escape the fatty deposits. Among these may be mentioned the subcutaneous tissue of the nose, lips, ears, and penis. The deposits are always in the connective tissues, so that the organs are in no wise disturbed. Extreme fatty deposits in the subepicardial tissue are said to weaken the heart's action.

METABOLISM.

Metabolism is the phenomenon of molecular exchange peculiar to living substance. All living beings exercise functions and thus expend energy, this energy costing them certain molecular alterations by which their tissues become changed and ultimately destroyed if no opportunity of reintegration is afforded them. Metabolism thus becomes one of the essential characteristics of life.

The metabolic processes while believed to be chemical are as yet inexplicable, and are inherent in and peculiar to living cells. Dead cells, even while enclosed in the body, manifest no such properties, and the cellular derivatives—intercellular substance—are *ametabolic*.

According to their nature, the metabolic processes can be divided into those which are constructive or integrative, called *anabolic*, and those which are destructive or disintegrative, called *katabolic*.

The *anabolic* processes are synthetic. Out of the nutrient materials distributed to them by the blood, the cells, through the aid of enzymes (?), build up more complex molecules.

The *katabolic* processes are largely analytic, and consist in the reduction of the molecules to simpler and simpler compounds until the "end-products" are reached. By the synthetic processes cytoplasm is formed and the numerous secretions of the body manufactured; by the analytic processes the complex molecules are transformed to water, carbon dioxid, urea, etc.

In ordinary normal cell life concomitant anabolism and katabolism are in continual progress, the exhausted cytoplasmic molecules being subject to immediate reintegration.

The cellular processes are associated with oxygen absorption and carbon-dioxid excretion, so that there is a constant gaseous exchange called *cell respiration*. In the normal condition a proper equilibrium between the oxygen supplied and carbon dioxid removed is maintained by the circulating blood; but in pathologic conditions this balance frequently becomes disturbed, and the ill effects of excessive or deficient oxidation becomes apparent.

Though in the condition known as asphyxia the effects of insufficient oxidation are easily recognized by the occurrence of carbon-dioxid poisoning, it is scarcely probable that the opposite condition—excessive oxidation—is analogous. Accelerated or excessive oxidation does not occur in consequence of an excessive absorption of oxygen, but from accelerated cellular energy, by which rapid oxidation of its molecules occurs. It is scarcely possible for the cells to receive an injurious oxygen supply, though they commonly suffer destruction in consequence of overactivity from quantities that may be below normal. The conditions in which oxidation of the cells becomes pathologic are *asphyxia* and *fever*.

Asphyxia or **suffocation** is an invariably fatal condition resulting from the combined effects of insufficient oxygenation and carbon-dioxid poisoning. No animal can live without oxygen, nor can any animal live in an atmosphere of carbon dioxid. In an atmosphere of carbon dioxid an animal dies almost immediately; but in an atmosphere without oxygen it dies almost as soon, presumably from carbon dioxid collecting in its own economy, though possibly from lack of oxygen.

When the simple forms of animal life are placed in an atmosphere of carbon dioxid, they become inactive and soon die. Upon the differentiated cells of the higher animals the poison behaves somewhat differently, acting first as a stimulant, then as a depressant. The effects of carbon-dioxid poisoning are well shown in the phenomena attending the death of one of the higher animals.

When the supply of oxygen is completely shut off the animal almost immediately becomes anxious, the respiratory movements accelerated, and the pulse quickened. As the carbon dioxid accumulates in the system the need of oxygen becomes more and more distinct, and more and more forcible expiratory movements are made until the animal is thrown into convulsions, that are succeeded by feebler gasping efforts, and finally by death.

It is customary to divide the phenomena of asphyxia into three stages: (1) That of exaggerated breathing, in which inspiratory efforts predominate; (2) that of convulsions, in which expiratory efforts predominate; (3) that of exhaustion.

The phenomena seem to depend upon poisoning of the nerve cells. As the carbon dioxid is inhaled, or accumulates in the blood, it acts upon the respiratory centers of the medulla oblongata, at first stimulating them to more forcible action and increasing the inspiratory efforts, so that more oxygen may be inhaled, next urging the muscles to forcible expiratory efforts, so that more carbon dioxid may be expelled. Finally the stimulation of the cells passes into depression as the poison keeps accumulating in the blood, and the cells die. It is interesting to observe that every muscle that can possibly lend the slightest assistance to the progress of respiration is called into action during asphyxia. Not only are the respiratory centers stimulated by the carbon dioxid, but the vasomotor and other nervous ganglia also become excited. During the first stage the vasomotor stimulation of the gas brings about the contraction of the arterioles, thus causing marked increase in the blood pressure. As the poison increases in the blood, it next produces stimulation of the pulmonary arterioles, preventing the right heart from readily driving the blood through them. The vigorous pulsations of the left heart succeed in driving the blood through the constricted arterial system to the veins, but the right heart experiences difficulty, because of its weaker wall, in forcing the blood through the pulmonary system. The obstruction to the circulation in the pulmonary vessels thus produced occasions distention of the right heart and pulmonary artery, together with a diminished flow of blood through the pulmonary veins into the left side of the heart. The heart ceases to beat in diastole, its cavities are full of blood, and its right side greatly overdistended. After death the blood passes from the left side into the arteries, so that at necropsies held upon asphyxiated individuals the right side of the heart and the great veins are greatly engorged with blood, though the left side of the heart is usually empty. The innervation of the iris is also affected and the pupil widely dilated. As the stage of exhaustion is reached the feces and urine may be spasmodically evacuated, showing that the nervous regulating mechanism of the bladder and rectum may be acted upon.

Dyspnea is a condition of accelerated respiration observed in many diseased conditions of the heart and lungs, in which, for mechanical reasons, the blood becomes charged with carbon dioxid. The quantity of poison in this condition is sufficient to stimulate the respiratory centers, though not to depress them. According to the severity of the condition, the accessory muscles of respiration are called into play. The blood is insufficiently oxygenated, and the bluish venous blood in the superficial vessels gives the skin, especially of the face, the lips, the finger-tips, and nails a purplish color (*cyanosis*).

It cannot be said with certainty that the degree of carbon-dioxid poisoning seen in dyspneic conditions is distinctly prejudicial to the cells of the body. The cells of the respiratory centers are probably, for obvious reasons, particularly sensitive to it.

Apnea is the opposite condition to dyspnea and asphyxia, in which it would seem that, as the result of forcible inspiration, an excess of oxygen had accumulated in the blood. It seems, however, to be a reflex phenomenon and not dependent upon oxygen alone, as when nitrogen, hydrogen, or other inert gases are so inhaled the same condition arises. The apneic condition is characterized by a period of rest succeeding forced inspirations, as if the quantity of oxygen that had been absorbed were sufficient to last for some time, so that further respirations become for the time being unnecessary.

There is no known condition in which too much oxygen is absorbed into the blood, as its hemoglobin and plasma seem capable of taking only so much of the gas, and even in atmospheres of pure oxygen can absorb no more. Should it be possible for unlimited oxygen to be absorbed, the acceleration of combustion might lead to speedy destruction of tissue. Though the oxidation of tissue is but slightly affected by the quantity of oxygen absorbed, other causes intrinsic in the organism may very markedly influence combustion, and not only occasion rapid tissue destruction, but also increase of temperature. This condition is seen in *fever.*

Fever is a term clinically used to describe conditions essentially characterized by increased temperature and accelerated combustion of the body. It is often spoken of as *pyrexia,* and is by many authors sharply differentiated from *hyperthermia,* which occurs in consequence of insolation, nervous lesions, and manipulations, and is characterized by increase of temperature, often to a point beyond that seen in fever, but by little destructive oxidation of the tissues. There is, however, no sharp line of differentiation, for in hyperthermia there is always some acceleration of combustion, and in fever its rapidity is variable.

Etiology.—Fever may be *traumatic* or *infectious.* *Traumatic fever* remains unexplained, but seems to be not infrequent after fractures of the long bones.

Infectious fever depends upon irritative micro-organismal products. Both animal and vegetable parasites may cause fever; thus, the malarial fevers, that are among the most frequent and severe, depend upon the hemameba, while typhoid fever, pneumonia, tuberculosis, etc., depend upon bacteria.

Hence there is no specific micro-organism of fever, which is to be looked upon as the result of irritative and usually toxic disturbance of the nervous centers concerned in heat regulation. Many infections are accompanied by thermotoxic irritation and many are characterized by mild fever. Those in which the toxic products have a specific affinity for the thermic centers are characterized by very high fever. The fever-producing poison being but one of the metabolic products of the micro-organism, it is easy to understand why fever may at times be very marked and at other times moderate in the same form of infection, varying according to the predominating product of the particular infecting organism.

Experimental fever may be produced by injecting peptones, albumoses, and other substances into the blood.

The **mechanism** of fever is complicated and variable. Knowledge of the subject, when sifted, seems to show that in all cases there is increased heat production, and in most cases diminished heat dissipation. The occurrence of fever, therefore, seems to depend upon irritation of the heat-regulating apparatus rather than upon the centers having to do essentially with thermogenesis or thermolysis.

The rise of temperature may be very slight (feverish) or may threaten the life of the individual (hyperpyrexia). The duration of fever varies according to its cause. In mild infections of short duration the condition soon passes away (ephemeral fever); in slow infections it may continue for weeks (continued fever). However mild or severe, ephemeral or continuous, it may be, it seems to furnish an excellent guide by which information concerning the progress of infection can be secured.

Certain **anatomic changes** characteristic of fever result from the accelerated combustion. Whether it is correct to speak of these changes as depending upon the fever is a question, for the elevated temperature alone is insufficient to bring them about, as is evinced by their absence in hyperthermia. It is not only possible, but highly probable, that these changes are not the result of the fever, but of accompanying phenomena, depending upon the same conditions as are responsible for the disturbance of thermotaxis. Thus, an intoxication stimulating the heat-regulating mechanism of the body may simultaneously bring about destruction of the red blood corpuscles, cloudy swelling of the kidney epithelium, irritability and hyaline degeneration of the heart muscle, and various similar changes. These, in turn, prevent the proper functional activity of the secretory and excretory glands of the body, with the result that the supply of useful secretions fails and the elimination of waste products is inhibited, so that the organism finds itself in a very abnormal condition, depending upon the intoxication rather than upon the fever, which is but one expression of the intoxication.

In fever nearly all of the tissues of the body suffer more or less change, either from direct toxic irritation or from involved morbid processes.

The *blood* usually shows that hemolysis is in progress, its erythrocytes being destroyed. Ughetti believes that the hemolysis is the essential feature of the fever. The urine is usually dark in color in consequence of the presence of blood pigment liberated from the red blood corpuscles. The alkalinity of the blood is usually diminished, and Minkowski has found lactic acid in the blood of dogs with experimental fever. The reduction of alkalinity is in proportion to the severity of the fever, and persists for some time after the temperature returns to normal. Increased alkalinity of the blood has also been observed by Biernacki. Leukocytosis is present in most fevers (see Leukocytosis), and fibrin is increased in some.

The *parenchymatous organs* are found after death to be in a state of cloudy swelling, and so regularly is this the case and so well does this condition explain the abnormal action of these organs that it seems proper to believe that cloudy swelling of the parenchymatous organs is constantly present in pyrexia. In exceptionally severe fever with hyperpyrexia, fatty metamorphosis of the parenchymatous organs is nearly always present.

The *heart* and *voluntary muscles* show degenerative changes chiefly of the hyaline form. The striations of the muscle fibers are lost, they break up into homogeneous masses and many of them disappear. In the heart muscle fatty degeneration not rarely occurs and may be the cause of death.

Concerning the whole body, there is no condition in which it wastes so rapidly as in fever. The fat is first absorbed and consumed, the muscular tissues next, and the glandular, connective, and nervous tissues last called upon to furnish the heat.

All the **functions of the body** are disturbed in fever. The *circulation* is usually accelerated, and the cardiac action may be so rapid as to prevent counting the pulse. Very rapid pulse is common in scarlatina; very slow pulse in typhoid fever. The cardiac action is also altered in rhythm by shortening of the diastole. The blood pressure varies according to the vasomotor excitation present, but is usually low.

The *respiration* is also accelerated, the normal pulse-respiration ratio usually being retained. The respirations may be shallow or deep. In the latter case the accessory muscles of respiration are called to action.

The *glandular secretions* are profoundly altered and universally diminished. The salivary glands pour out a scanty, thick secretion, so that the mouth becomes dry and the patient suffers from thirst. The gastric juice is said to be reduced in amount and its acid lessened, so that proteid digestion is embarrassed. The liver being in a state of cloudy swelling, probably less bile than normal is secreted. The absence of the usual quantity of bile, together with diminished secretion of intestinal juice, cause constipation, except where some other condition is present to occasion diarrhea.

The *skin* is hot and dry in fever and the secretion of sweat suppressed. This gives the skin a hot, dry, pungent feel. Sweat may be abundantly secreted during crisis or during intermissions.

The *urine* is scanty, dark colored, and of high specific gravity. In most cases it contains small quantities of albumin, and may contain tube casts. The potassium salts are usually increased and the chlorids diminished. Various abnormal urinary ingredients present themselves under the varying conditions met in fever. Among these may be mentioned albumoses, where destruction of tissue is in progress; acetone, diacetic acid, and oxybutyric acid. An increased proportion of sulphates is present, as well as an increase of phosphorus. In typhoid fever and some other slow febrile processes diazobenzophenosulphonic acid may be present, giving the "diazo reaction" of Ehrlich.

The *mammary secretion* is both diminished in quantity and altered in quality, as nursing infants often become ill from the milk of a febrile mother.

The *nervous system* suffers, sometimes from the very beginning of fever, the symptoms being headache, vague pains in the back and extremities, delirium that may be wild and maniacal or low and muttering, accompanied by *subsultus tendinum* (twitching of the tendons in their sheaths) and *carphologia* (a tendency to pick at and draw up the bedclothes).

The *metabolic processes in fever* are very interesting, and a study of the excretions shows exactly what is taking place in the tissues of the patient.

Study of the respiration shows that the discharge of carbonic acid and absorption of oxygen are greater in the initial stages of fever than in health. During the fastigium and throughout the period of decline this varies but little from the normal.

The renal secretion shows that the excretion of nitrogen (urea) is far greater in fever than it is in health upon the same diet, this increase beginning before the rise of temperature and ceasing with its decline. It is the index of proteid destruction in the body. The alloxuric bases are also all increased, indicating destruction of nucleo-albumins as well as other proteids.

SECRETION.

Secretions are fluid or semi-fluid products of cellular activity, produced chiefly by the epithelial glands and intended for further use in the economy. Secretions differ from excretions in that the latter are of no further use and are formed solely for removal from the body ; but the distinction is often difficult to make, because some glandular products, like the bile, are both secretory and excretory in nature. Both secretions and excretions are elaborated by the cells from materials obtained from the blood.

Secretions may be *external* or *internal*. *External secretions* are conveyed from the glands by ducts in order that they may immediately perform their functions, as in the case of saliva, gastric and pancreatic juices, bile, milk, etc. *Internal secretions* are retained within the glands, to be slowly absorbed from them for distribution by the blood. The ductless glands all have internal secretions, and it seems probable that the pancreas, the liver, and the sexual glands may have both external and internal secretions.

Concerning the external secretions, the saliva, gastric juice, pancreatic juice, bile, and succus entericus have already been mentioned in their relation to digestion. The mammary secretion is intended only to supply nourishment for the offspring, so need not be particularly discussed. The important internal secretions are formed by the thyroid, pituitary, adrenal, pancreas, liver, and sex glands.

The **thyroid secretion** exerts a very pronounced effect upon nutrition. When the thyroid gland is completely extirpated from dogs and cats the animals soon develop an illness characterized by muscular tremors, weakness, tetany, convulsions, and fatal cachexia. Total extirpation of the gland in man produces similar effects. The patient loses in mental and bodily vigor, becomes weak, his temperature is reduced and he is chilly; there are pains in the arms and legs, the skin becomes thickened and the hair falls out, the eyes water and the speech becomes slowed. If in operating either upon man or the lower animals the extirpation of the gland is not complete, but a small fragment is left, the untoward symptoms either do not develop or are greatly delayed ; and in cases in which total extirpation has been performed, the development of symptoms may be prevented or delayed by the occasional subcutaneous injection of an extract of the glands, or by eating the glands removed from food animals. These facts lead us to conclude that the secretion of the gland is slowly absorbed by the blood and controls the nutritive conditions of the body. When, through disease of intra-uterine life or of infancy, the thyroid gland fails to develop or is destroyed, the child never grows in the normal manner, but becomes an imbecile dwarf, with short legs and arms, prominent belly, soft white skin, mucous deposits in the subcutaneous fatty tissue, thick lips, large tongue, puffy eyelids, etc., known as a *cretin*.

A sporadic or occasionally endemic form of cretinism known as *myxedema* is occasionally seen in adults suffering from operative removal, atrophy, or enlargements of the thyroid gland, or, as such enlargements are called without reference to their nature, *goiter*. Women are more frequently affected with myxedema than are men. The disease is sometimes hereditary. It is characterized by increased bulk of the body and firm, inelastic swelling of the skin, especially of the face. The skin over these swollen areas is white, is not indented by pressure, and the lines of expression are changed and often obliterated. There may be subcutaneous swellings about the roots of the neck. The hair is imperfectly nourished and not infrequently falls out. There is considerable mental deterioration—loss of memory, irritability, and in some cases delusions and hallucinations. That the thyroid substance is concerned both in cretinism and myxedema is shown by the fact that both conditions improve and may recover under thyroid medication.

In **exophthalmic goiter** we see the opposite condition from that bringing about cretinism, characterized by enlargement of the thyroid gland, paroxysmal attacks of cardiac palpitation, exophthalmos, and nervous excitement. These appearances suggest that the symptoms depend upon the entrance into the blood of an excess of thyroid secretion, but though upon purely theoretic grounds this seems quite reasonable, there are reasons for doubting it. Thus, there is no experimental evidence that thyroid secretion can produce exophthalmos. Sollier has also shown that rare cases of combined myxedema and exophthalmic goiter occur, involving the physiologic paradox of the secretion being absent or diminished so as to permit of the occurrence of myxedema, yet increased so as to cause exophthalmic goiter. The true relationship between the thyroid gland and exophthalmic goiter, therefore, remains a question.

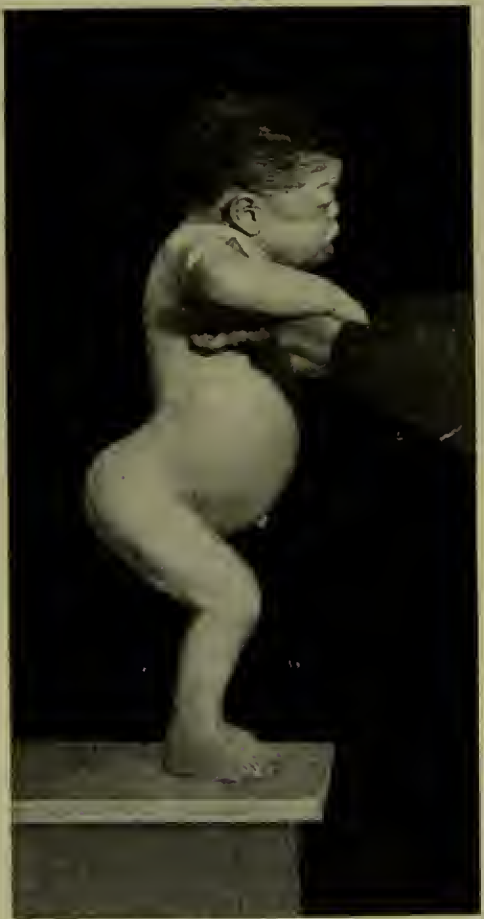

FIG. 31.—Cretin.

What the important ingredient of the thyroid substance is has not yet been fully determined. Baumann found that if sheeps' thyroids are boiled for twenty-four hours with 10 per cent. sulphuric acid, the active principle is not destroyed, but that the substance precipitated after cooling such a decoction contains nearly 10 per cent. of iodin. This iodin seems to be contained in the colloid substance, and the name "thyroidin" has been suggested to express the active principle of the glanduiar secretion.

Pituitary Secretion.—The exact nature and true office of this secretion has not yet been determined. Some relationship seems to exist between it and the thyroid gland, both secretions exerting a marked and important influence upon nutrition. Accumulating experience seems to corroborate the view that the interesting affection known as *acromegaly* is dependent upon disease of the pituitary body. Whatever the relationship between them may be, the pituitary body is diseased in nearly all cases of acromegaly. In many cases there is associated disease of the thyroid. In *giantism* also, as shown by Hinsdale and others, the sella turcica is large and the pituitary body larger than normal.

Acromegaly is a disorder of nutrition, characterized by enlargement of the bones of the face and extremities. The features become large and coarse, the malar bones and jaw unduly prominent and the face ponderous. The hands and feet grow to a remarkably large size and are obviously disproportionate to the rest of the body. There are associated constitutional symptoms, and the patient suffers from headache, sweating, and lethargy. The speech may be thick and the memory impaired, but the intelligence is usually unaltered or but slightly blunted. Blindness sometimes occurs, probably when the disease of the hypophysis extends to the optic tracts.

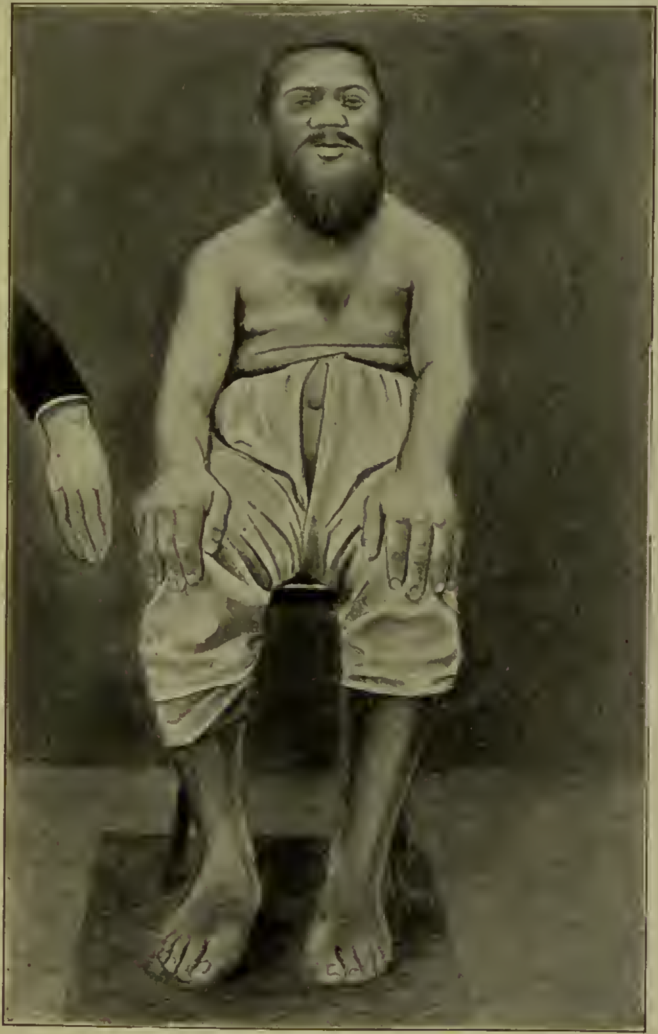

FIG. 32.—Man aged twenty-eight years with acromegaly (Sternberg).

The enlargements are true hypertrophies, embracing all of the tissues of the affected members, even the bones, which become roughened on the exterior and somewhat rarefied.

The **pancreatic secretion,** in addition to its digestive enzymes—trypsin, steapsin, and amylopsin—seems to contain a *glycolytic ferment* that may act in one or the other of several ways. It may influence the production of sugar from glycogen by its action upon the liver cells, or the production of glycogen from dextrose by its action on dextrose, or the tissues of the body, so that they consume the dextrose from the sugar.

Diabetes.—Diabetes is a disease characterized by an erroneous treatment of carbohydrate foods, which, although properly digested and absorbed, are not utilized for the generation of force by combustion, or stored up in the form of fats and glycogen, but are immediately eliminated by the kidneys in the form of sugar.

The presence of sugar in the urine is the essential feature of diabetes, though it occurs in other conditions that must be carefully differentiated from it. The first of these is *alimentary glycosuria* and is seen in healthy individuals after excessive consumption of carbohydrates, especially sugars. The excess of sugar being beyond what the economy can dispose of by combustion or glycogen transformation, accumulates in the blood (*glycemia*) and readily passes into the urine (*glycosuria*). This condition is, however, a temporary one, and its cause is easily determinable.

Shock may also cause glycosuria. It is so certain to produce it, that scarcely any further manipulation of a dog is necessary than to secure it to an operating-table before sugar makes its appearance in the urine. The majority of severe operations are succeeded by it. An invariable glycosuria results from puncture of the floor of the fourth ventricle of the brain, the so-called *picquer* of Claude Bernard. When this puncture is made, glycosuria comes on very quickly. In from thirty to forty minutes the amount of sugar in the blood is found to be doubled or trebled, and sugar is present in the urine.

The maximum amount of sugar occurs in about an hour, after which it diminishes and disappears in five or six hours. Bernard never found it continuing more than twenty-four hours. Though the floor of the fourth ventricle seems to be the part of the nervous system best adapted to the experimental production of glycosuria, injury of other parts of the brain, spinal cord, and peripheral nerves may do so. There is no known injury of the nervous system that is succeeded by permanent glycosuria.

The *effect of certain poisons and drugs* may lead to glycosuria resembling diabetes, but fungacious in character. Of these may be mentioned curare, chloroform, ether, carbonic acid, morphia, chloral, corrosive sublimate, turpentine, and phloridzin. The poisoning by phloridzin is interesting because it leads to the excretion of about one hundred times as much sugar as could be formed by its own disintegration.

The *removal of the pancreas* invariably leads to glycosuria that more closely approximates diabetes than any of the others, because of its persistence and ultimately fatal outcome. The condition develops only when the entire pancreas is extirpated. If a small portion be left, or if a fragment of the organ be transplanted to the subcutaneous tissue, no diabetes develops, although at any subsequent period its occurrence can be determined by extirpating the fragment. This fact disproves the view held by some that pancreatic diabetes depends upon the injury done to the sympathetic nerves during the operative removal of the pancreas.

Senility is sometimes accompanied by a glycosuria that closely resembles and may be a mild form of diabetes.

Though it is true that the various glycosurias induced by the means described all resemble diabetes to a more or less perfect extent, with the exception of the last two, they all differ in the fact that *in diabetes alone the condition is progressive and persistent.*

A diabetic is in most respects quite normal until late in the disease. The appetite is good and commonly excessive, for the reason that while an abundance of food is taken by the patient, comparatively little is used. The thirst is excessive and large quantities of fluids are consumed. This is also easily explained, as the patient is passing excessive quantities of urine, and the greater the quantity of urine passed the greater the need of water becomes. The large quantity of urine passed is less easy to account for, though it can be experimentally shown that the presence of sugar in the blood is always associated with an increased secretion of urine, so that the sugar itself may be responsible for it.

When the metabolic processes are estimated by studying the end-products, we find that in diabetes the relative intake of oxygen and output of CO_2 is about normal, or that there is a moderate increase of CO_2 in the expired air, indicating that carbohydrates are not being consumed. The urine always contains a great increase of urea, but a study of the diet of the patient shows that it consists essentially of proteids, and that the normal balance of proteid metabolism is not disturbed. In most cases the excretion of urea is thoroughly commensurate with the quantity of proteid consumed. The proteid consumption may, however, be subject to certain paroxysmal exacerbations, as when a patient, having abstained for a time from carbohydrate foods, suddenly indulges and suffers from a sudden great increase in the quantity of sugar in the urine, and of urea as well.

The characteristic feature of the disease is the occurrence of sugar in the urine. This glycosuria is always preceded by glycemia, or increase of the sugar in the blood. Normally the blood contains 0.1 per cent. of sugar, of which an extremely small and usually unrecognizable amount passes into the urine. In severe diabetes the patient may pass as much as 4 liters of urine, containing 250 gm. of sugar each day.

The sugar present in diabetic urine is always dextrose, regardless of the form in which the sugar is consumed—whether as dextrose, saccharose, lactose, maltose, or as starch. In alimentary glycosuria this is not true, for if dogs are given an excess of levulose, both dextrose and levulose appear in the urine, and the same is true of galactose.

The respiration, circulation, and digestion of the diabetic are not changed. The occasional errors of digestion are probably accidental and coincidental rather than significant. The excretory powers are also unchanged, except as influenced by the excessive glycemia. The disease, therefore, so far as its physiology can be determined, is one of metabolism.

The *morbid anatomy* of the affection is extremely simple. The *liver* is usually enlarged and somewhat congested. The cells of the parenchyma usually contain an excess of glycogen irregularly scattered about. So marked may be the glycogen deposits and so irregular their distribution that some claim to be able to recognize the liver of a diabetic by its microscopic appearance alone. In the late stages of the disease the glycogen may be absent.

The *kidneys* are frequently the seat of an acute parenchymatous degeneration that is probably caused by the persistent glycosuria. It is interesting to observe that when albuminuria occurs in diabetics the glycosuria frequently lessens. The epithelial cells of the kidneys usually contain large drops of glycogen, and sometimes the tubules are dilated with material giving the microchemic glycogen reaction.

The *pancreas* is rarely grossly diseased in diabetes, the abnormal condition sometimes, as in interstitial pancreatitis, appearing to be of some etiologic importance, while in other cases, as carcinoma, it is very doubtful.

No other organs are the seat of important lesions, though they may show varying pathologic changes associated with the disease. The skin, for example, may be the seat of local patches of gangrene, and commonly shows Xanthoma diabeticorum and other lesions. From the lesions described, the only organs that need concern us in seeking for the cause of diabetes, are the liver, kidney and pancreas.

The *liver*, as is well known, is one of the storehouses of the carbohydrate reserve supply retained in the form of *glycogen.* Probably the first to point out the possible association between the liver and diabetes was Claude Bernard who taught that the carbohydrates were stored in the liver in the form of glycogen, and that under proper stimulation, the glycogen was transformed to sugar and supplied to the blood. If from any cause, such as nervous puncture, the liver becomes congested, the conversion of glycogen to sugar was facilitated and hyperglycemia caused. If for any reason the congestion of the liver became permanent, diabetes resulted. This theory was criticised by Cohnheim and others, who doubt that sugar is always formed from glycogen; who find that glycogen is stored in the muscles and other tissues as well as in the liver; who bring forward evidence to show that sugar may be formed from proteids; and who find no experimental evidence to show that increased rapidity of the flow of blood through the liver can be produced by the puncture of the floor of the fourth ventricle.

Bernard believed that in the normal nutrition of the body the sugars were carried by the portal blood to the liver and were there converted into glycogen, in which form they were retained until needed, when they were again transformed to sugar and thrown into the blood. It has been found, however, that though it may be true that the liver is important in dealing with sugars, its function is not indispensable in that particular, for if an Eck's fistula be made between the hepatic and portal veins, so that the sugars of the portal vein reach the systemic circulation without passing through the liver, no diabetes develops in the dogs so treated.

What becomes of the sugar under normal conditions is a problem of great importance, concerning which we are still somewhat in the dark. The evidence seems to indicate that it is oxidized in the functionating cells of the body, wherever needed, and not consumed in some one place, as, for example, in the lungs, as Liebig formerly thought. What is not so destroyed is probably transformed to fats and glycogen, and stored in various of the tissue cells.

Diseased kidneys have been thought by many to be the source of diabetes, but the improbability of this is shown by the fact that the glycosuria—the only symptom calling attention to the kidney at all—is only a natural consequence of the hyperglycemia for which the kidney cannot possibly be responsible.

The *pancreas* must bear a very important relation to diabetes, as its extirpation is so invariably followed by fatal diabetes in the lower animals, and its diseased condition by occasional diabetes in man. In many cases however, no macroscopic lesion of this viscus is found. It has been shown experimentally, as has already been mentioned, that if when the pancreas is removed a fragment of its tissue be implanted beneath the skin no diabetes follows, although the subsequent excision of this fragment permits its development. This suggests that the pancreas not only secretes the well-known "juice" that it pours through Wirsung's duct into the duodenum, but that it has also an internal secretion that can still be utilized, although but a fragment of the organ remain and occupy an abnormal position in the body. The nature of this probable secretion is unknown to us, as is also the seat of its elaboration. The pancreas contains peculiar elements—the islands of Langerhans—the function of which has long been a question, but which may be the source of the secretion. Opie has lent support to this view by showing that in 11 cases of diabetes, studied changes were present in the islands of Langerhans in nearly all.

Theory of Diabetes.—Many theories have been advanced at different times to explain diabetes, but our knowledge of the disease is still imperfect. It must depend either upon an increased production of sugar in the body or upon a diminished consumption of sugars taken into it. Those who hold to the former view see the sugar formed from the glycogen of the liver and muscles, and later from proteids. There is evidence to show that sugar can be made from proteids, and Cohnheim was so persuaded that it was the rule in diabetes that he wrote, "The question is not whether carbohydrates *or* albuminous bodies are the antecedents of the glycogen ; we can at most discuss the possibility that *besides albumin*, *other glycogen builders exist.*" The theory of Claude Bernard that the liver is at fault—the *vaso-hepatic theory*—can surely be dismissed after the evidence already cited to show that shutting the liver out of the circulation does not cause diabetes; that experimental diabetes produced by the *picquer* is not associated with recognizable hepatic changes; and that extirpation of the pancreas in animals with healthy livers does produce diabetes.

The *oxidation theory* of Ebstein and Van Noorden explains diabetes by supposing that the patient fails to oxidize sugars in his tissues and transform them into CO_2 and H_2O. It is true that the CO_2 production in diabetes is lower than normal, but it can be explained on the ground that while there is a failure to oxidize sugars, fats and proteids are oxidized with less CO_2 output than sugars would yield. Thus it appears not that oxidation is defective, but that the oxidation of sugars is defective. It surely does not explain diabetes to show that in diabetic metabolism sugars are not oxidized.

The *nervous theory*, or *neurosecretory theory*, has a rather substantial foundation in the experimental evidence accumulated. The *picquer* of Claude Bernard with its succeeding glycosuria, the operative glycosuria, the occurrence of diabetes after shock, nervous strain, and injuries, together with the fact that stimulation of the peripheral end of the splanchnic nerves causes glycosuria, all show that nervous impulses control the sugar metabolism to a certain extent, though other circumstances prevent us from believing that the nerves are in most cases directly concerned in the occurrence of diabetes.

The *ferment theory* was first suggested by Cohnheim, who, after a careful analysis of the conditions occurring in diabetes, concluded that "everything considered, it appears to me much more probable that the diabetic consumes less sugar owing to the absence of a ferment which, in a normal condition, initiates the further decomposition of sugar."

This theory, advanced nearly a quarter of a century ago, meets with most favor at the present time. The nature of the ferment, however, is unknown. It may, as Cohnheim suggests, operate by glycolitic action, or it may act in the opposite manner by synthetizing the sugars to higher and more useful compounds. The experiments of von Mehring and Minkowski, who have shown that extirpation of the pancreas produces diabetes in the lower animals, lead us to infer that the enzyme is formed in the pancreas, and the number of cases of diabetes with associated pancreatic lesions in man partially confirms this. Noting that a fragment of the pancreas retained in its normal position or transplanted beneath the skin prevents the occurrence of diabetes, we can surely conclude that the enzyme is an internal secretion of the pancreas, having nothing to do with the digestive secretion of the organ. Looking for the origin of this internal secretion, we find the islands of Langerhans scattered throughout the organ to be of no known function, to be without communication with the ducts of the organ, to be epithelial in structure and not unlike other of the ductless glands in certain particulars, and it was easy for Opie to draw the inference that this internal secretion of the ferment that has to do with the transformation and utilization of sugars in the body is produced in these islands of Langerhans in the pancreas. Unfortunately, however, changes have not been found in these structures in all cases of diabetes.

The **adrenal bodies** seem to elaborate an internal secretion of great importance, as its loss from removal or destruction of the glands is followed by increasing prostration, collapse, and death in from a few hours to three days. When the destructive disease is slow in operation, as in tuberculosis and carcinoma, the increasing weakness is accompanied by a disturbance of the dermal pigmentation by which the skin of the face, hands, arms, and other parts of the body, and sometimes of the whole body, becomes bronzed either uniformly or in streaks and blotches. This symptom of *Addison's disease* leads us to infer that the adrenal bodies have charge of the pigment regulation of the body, though experiments, especially when performed with extracts of the gland substance, show a more conspicuous effect upon the vascular tone. When adrenal extract is applied locally to the tissues it causes contraction of the vessels with which it comes in contact, and when injected into the circulation increases the blood pressure by causing contraction of the arterioles through its direct action upon their muscular tissue.

The **sexual glands** undoubtedly exert some influence upon the nutrition of the entire organism. Of what nature it is, and whether or not it can properly be looked upon as an internal secretion, we are yet in the dark. The evidence shows, however, that some substance is present or formed in those glands that influences growth, health, spirit, and vigor while present, and occasions change of disposition and alteration of structure when lost. As examples of this may be mentioned the unusual development that takes place in unsexed cattle, the heavy-set bull, with his short, thick neck and powerful short horns, contrasting with the more slender limbs and neck, fatter body, narrower head and shorter horns of the sexless ox. The large size and corpulence of dogs and cats after early castration is well known. The effeminate eunuch is of unusual stature, and has a high-pitched voice, as contrasted with the sexually perfect man. In women whose sexual organs are hypoplastic a masculine development often occurs, the body being large and muscular, the voice powerful, and the face hirsute. Women whose sexual organs cease to exert their normal influences in consequence of disease or operative removal, suffer from the physiologic changes characteristic of the menopause, succeeded by loss of sexual desire, development of self-assertiveness, sometimes to the degree of masculinity, corpulence, and occasionally a growth of hair upon the lip.

EXCRETION.

Excretion is the process by which effete material is eliminated from the body. With the exception of such insoluble substances as may be contained in the food or otherwise find entrance into the alimentary apparaus, everything of which the body consists and upon which it subsists reaches it in the fluid condition, being first dissolved by the digestive juices and then absorbed into the blood. It is likewise into the blood that the products of cellular metabolism are poured, and, therefore, from the blood that they must be removed. The excretions, with the exception of the carbon dioxid that escapes from the lungs, are the products of cellular activity, being formed in glands specially designed for the purpose. An excretion is a waste product. It is something eliminated as useless. The usefulness and uselessness are the criteria for differentiating secretions from excretions. Sometimes a gland may perform simultaneously the functions of secretion and excretion. Thus, the liver is supposed to furnish in the bile substances *secreted* for the purpose of aiding the absorption of fats, and at the same time substances *excreted* as of no further use—urea, biliverdin, etc.

By study of the excretions one obtains an index to the metabolic processes, as the quantity of waste products they contain depends upon the activity of combustion in the body. Under normal conditions the excretion corresponds in proper proportion to the food consumption. Under pathologic conditions it may be greatly in excess, indicating that in addition to the food consumed the tissues of the body are being oxidized; or may be diminished, showing that waste products are being retained to the detriment of the individual.

The study of the excretions necessitates a consideration of the expired air, the urine, the sweat, and the bile.

Pulmonary Excretion.—When the respiratory movements take atmosphere containing oxygen into the lungs, some of the gas is retained and combines with carbon to form carbon dioxid, and with hydrogen to form water; so that the expired air contains a diminished quantity of oxygen and an increase of carbon dioxid that escapes into it from the blood. The gaseous interchange, by which is meant the proportion of the absorbed oxygen to the eliminated carbon dioxid is expressed—$\frac{\text{Volume of } CO_2 \text{ excreted}}{\text{Volume of O absorbed}}$—and called the *respiratory quotient*. At one time this respiratory quotient was thought to be fixed, but it is now known to be subject to marked variations according to the particular diet consumed, according to the amount of work the individual performs, and according to the frequency and depth of his respirations. The respiratory quotient is highest—that is, the quantity of oxygen absorbed is least, where the possibilities of numerous combinations are least. Thus, upon a carbohydrate diet, where the oxygen has to combine with carbon only, the respiratory quotient is 1; upon a diet of fats, where the oxygen combines with carbon to form carbon dioxid, and with hydrogen to form water, it is lower, being approximately 0.7; while upon a diet of proteids, where it has more numerous combining opportunities, it is lowest, it may go as low as 0.65.

The study of carbon-dioxid excretion has not thrown much light upon pathologic processes, and is a matter to which, in consequence, comparatively little attention is paid by clinicians. Indeed, as man lives upon a mixed diet, his usual respiratory quotient is about 0.85, and variations from this in disease are usually toward a lower point, because as the result of disease the patient usually consumes his own proteids. In cases of prolonged fasting with consumption of the body proteids after the fat was exhausted, the respiratory quotient has been found at 0.65.

Urinary Excretion.—The urine, the excretion of the kidneys, removes from the body the greater part of its surplus water, numerous mineral substances, such as sodium chlorid, phosphoric acid, sulphuric acid, ammonia, and salts of potassium, calcium, and magnesium. Far above these in importance, however, are certain organic substances whose presence depends not upon their surplus ingestion in the food, but upon metabolic processes that take place in the tissues. Of these *urea*, CON_2H_4, is the most important, uric acid $C_5H_4N_4O_3$ next. Kreatinin $C_4H_7N_3O$ rarely becomes important.

The water of the urine escapes by transudation through the capillary walls of the glomerules; the solids are for the most part secreted by the epithelial cells of the uriniferous tubules. The regulation of the quantity of watery constituent depends upon the blood pressure, which when elevated, either throughout the whole arterial system or locally in the kidney, increases the transudate, and when lowered diminishes it. The cells of the glomerule, however, are of importance, and their selective tendency is well shown in the fact that only certain substances, dissolved in the blood, are permitted to pass through.

That the epithelium is the essential secreting part of the organ is not only suggested by its quantity, but is proved by experiment. Heidenhain found that when sodium sulphoindigotate was injected into the blood, it was found to have colored blue only the cells of the convoluted tubules of the kidney, proving that it had some particular affinity for those cells. Batrachians have a double blood supply to the kidneys, one through the renal arteries supplying the glomeruli, the other through the renal-portal vein supplying the convoluted tubules. Nussbaum showed that when certain foreign substances, such as peptones and sugars, were injected into the circulation of the frog, they were eliminated, even though the renal-portal vein was ligated, by the glomeruli. When urea was injected into the circulation, it was eliminated from the renal-portal blood, even though the renal arteries were tied. Kirk points out that if the cortical substance of the kidney containing the glomeruli be cut away, the secretion of urea continues because of its secretion by the epithelial cells.

The daily average quantity of urine secreted by a healthy adult is about 1500 c.c. The liquid is clear and amber colored, devoid of sediment, acid in reaction, and has a specific gravity of 1020.

I. The *quantity of urine may be increased* (*polyuria*) or diminished (*oliguria*), or suppressed (*anuria*). The quantity of urine excreted depends chiefly upon the blood pressure. If the blood pressure is high, other things being equal, the quantity of urine secreted will be large. Excessive consumption of fluids, necessitating removal of large quantities of water, causes polyuria. The relation of fluid to be eliminated to quantity of urine depends to a certain extent upon the activity of the skin, which, in its turn, is actively affected by external temperature, etc., so that in cold weather, the skin being inactive, more urine is excreted than in hot weather, when the skin is covered with perspiration.

In diabetes there is marked polyuria. The administration of certain drugs, such as digitalis, caffein, spartein, etc., produces increased excretion of urine (*diuresis*), usually by increasing the blood pressure, though sometimes by acting upon the secreting parenchymatous structure.

II. The *quantity of urine may be reduced* in a variety of conditions, of which the most frequent is probably *fever*. Disease of the kidney from degenerative and sclerotic changes of its substance leads to scanty urine. When the quantity of urine is great the specific gravity is usually low, the exception to this being in diabetes, where, because of the large quantity of sugar the urine contains, it may reach the high mark of 1040 in spite of its great quantity. When the urine is scanty the specific gravity rises from the altered relation of fluid to solids.

III. The *secreted urine may be retained* in the body because of obstruction of the urinary passages by strictures, calculi, neoplasms, ligatures, etc. The ultimate outcome of such cases being uremia, preceded by structural changes depending upon the accumulation of fluid in the pelvis of the kidneys, ureters, bladder, etc.

IV. The *secretion of urine may be checked or suppressed.* This always depends upon disease of the secreting substance of the organ, and is the most serious of all urinary troubles, being invariably fatal in continued cases. Death in these cases is said to be due to *uremia*.

Uremia, signifying urea in the blood, is a term used by clinicians to describe certain symptoms supervening upon sudden or gradual cessation of urinary excretion. According as its development is sudden or insidious, it may be described as acute or chronic.

Acute uremia is characterized by the rather sudden development of epileptiform convulsions, unconsciousness, vomiting, headache, and blindness.

The convulsive seizure may be the first intimation of the disease, or the patient may first endure a period of headache, vertigo, and sickness at the stomach. Death occurs in coma with frequent convulsions.

Chronic uremia usually progresses slowly, with headache, vertigo, drowsiness, and diarrhea. Sometimes there is vomiting; there may be asthma. Sooner or later coma comes on. Sometimes there is a period of semi-coma, from which the patient can be aroused and for a time is intelligent, but soon lapses again into stupor and unconsciousness. Cheyne-Stokes respiration is common in this coma and precedes death.

The original view concerning the pathology of uremia was that it depended upon the presence of urea in the blood. Urea is formed in the final metabolic changes of protoplasm. It is derived in very small part from the food, almost the entire amount present in the urine being the result of metabolism. It is chiefly through the urea that the body rids itself of the accumulating effete nitrogenous materials. It is not yet positively determined where urea is formed, but it is probably in the liver. The antecedents of urea are probably discharged into the blood from all of the active metabolic tissues, thus, in the striped muscular tissue, one of the antecedents of urea, known as kreatin, is formed as the result of its metabolism. This is by a simple change converted into kreatinin, which is a substance excreted by the kidney. There is, however, much kreatin in the muscles, but very little kreatinin in the urine—no more, in fact, than can be accounted for by the consumed food. When we inquire what becomes of the kreatin, it seems highly probable that when carried to the liver it is transformed to urea.

The average quantity of urea present in the normal urine is about 2 per cent.

Being so important an excrementitious substance, it was early inferred that its retention in the body would cause the symptoms of uremia, but the experimental evidence of this is still lacking, for we find that animals can endure the injection of enormous quantities of urea into the circulation without such symptoms. We find, however, that the same thing is true of the urine itself, which can be endured without much inconvenience. The explanation may be, however, that these substances are endured only while on the way to rapid elimination, for no sooner are they introduced into the blood, than they are eliminated by the kidneys. It is at first a paradox that an animal should be unable to endure the effect of the accumulation of its own excrementitious products, though it can bear the injection of the urine of another into its blood. The elimination must explain this, as we find that when an animal's kidneys are removed, it dies in two or three days from uremia; but that if, after the kidneys are removed, or thrown out of service by ligation of the renal artery, urine previously passed by itself or some other animal is injected into it, the fatal termination is greatly hastened, and that a large quantity may cause death in a few hours. Uremia develops in all cases of extirpation of both kidneys, ligation of the renal arteries, and ligation of the ureters.

In all cases of uremia the urea of the blood is increased. In animals whose kidneys have been thrown out of service, the injection of urea does not produce anything like the result produced by the injection of the urine itself into the blood, so that though urea may be one of the uremia-producing substances, it does not seem to be the most important one.

Frerichs supposed that the symptoms of uremia depend upon the presence of *ammonium carbonate* formed out of urea by some ferment in the blood. It has since been shown, however, that the only place that such a transformation can take place is in the intestine, and that its effects are purely local and not provocative of uremia.

Experimental work upon dogs with Eck's fistulæ has shown that in the animals whose livers are put out of use by the communication between the portal vein and vena cava, symptoms of uremic poisoning slowly develop. If about the tenth day they are given a meal of proteid food, an attack that is quite typically uremic comes on and may be fatal. The urine of such dogs contains less than the normal quantity of urea, though the kidneys are normal and free to excrete whatever urea is in the blood. The inference is that the blood is not surcharged with urea. The urine always contains an increase of uric acid, ammonia, and carbamic acid, the excretion usually taking place as ammonium carbamate. It is known to chemists that amido acids, such as carbamic acid, occur by hydration of proteid substances in the body and can be further changed to urea. The thought suggested by this knowledge is that the liver being incapable of acting upon those substances that it transforms into urea, they, and chief among them carbamic acid, accumulate in the blood, poisoning the animal and ultimately occasioning its death.

From this point of view the symptoms of uremia depend not upon the urea itself, but upon its unconverted antecedents, and especially upon *ammonium carbamate.*

V. *The removal of excrementitious substances by the urine may be imperfect.*

Under this caption may be considered certain conditions that never develop in consequence of total suppression of urine, cannot be produced experimentally, and that seem to be the result of continuous slight defects, of metabolism and elimination, not of sudden serious ones. The most important condition of this kind is *gout.*

Gout is a disease depending upon errors of metabolism, by which, either because of excessive formation or diminished elimination, uric acid and its compounds are deposited in the tissues, especially in the articular cartilages.

The relation of gout to uric acid is certain, though by no means clear. The disease is essentially characterized by more or less extensive depositions of sodium urate in the affected tissues. The usual seat of election for this deposition being the articular cartilage of the metacarpophalangeal articulation of the great toe. It is supposed that this joint is so commonly affected because of frequent mild traumatic injuries that it receives. This is, however, not certain, though it has been observed that when other joints have been injured, they are apt to be the seat of gouty deposits.

Sometimes the salts are deposited in the cartilages of the nose and ear, forming circumscribed enlargements described as *tophi.* Tophi may also occur upon the palms of the hands, soles of the feet, the eyelids, the sclerotic coat of the eye, and in the cerebral and spinal meninges. Gouty deposits also occur in the fibroconnective tissue of the kidneys, and in the medullary portion, where they appear as stripes running parallel with the tubules.

In the tissues the gouty deposits usually occasion sufficient local irritation to predispose to connective-tissue formation. In the joints, where the quantity of the salt is greater, they form a mortar-like mass, which, when microscopically examined, proves to be made up of acicular crystals of sodium urate. There is nearly always some superficial necrosis of the cartilage, and some writers have supposed that it is because of a primary necrosis that the crystals of the salt have been precipitated. It seems more reasonable, however, to conclude that the necrosis occurs in consequence of the pressure of the irritating crystals. The pain so characteristic of the affection is easily explained by the denudation and roughening of the cartilages.

The result of the gouty deposit is that the joints become greatly enlarged and deformed. Excessive uratic deposits may work their way through the superficial tissues and appear as chalky masses upon the surface. The irritative action of the salts seems further proved by the fact that gout is nearly always associated with a general tendency to fibrosis, and nearly always accompanied by arteriosclerosis, fibroid or cirrhotic kidney, and other allied conditions.

Gout is apt to be a family disease, showing marked heredity. In gouty families some individuals suffer from the typical gout of the great toe (*podagra*), while others show the inherited predisposition in lithemia, calculus, neurasthenia, arteriosclerosis, chronic interstitial nephritis, epilepsy, and a variety of other affections that experience refers to the presence of some irritating substance, presumably the compounds of uric acid in the blood. To these conditions the terms *lithemia* and *uratemia* have been applied.

Gout usually makes its appearance after middle life, and is usually a disease of the affluent. High living, plenty of wine, and lack of exercise greatly predispose it. Because of their excesses men seem to suffer more frequently than women.

It is a paroxysmal affection, characterized by outbursts of violent headache, depression, anorexia, fever, and irritability, during which the patient's intelligence seems to be clouded, followed after some days by a sudden excessive exacerbation of the local lesions of the affected joints and immediate improvement of the constitutional symptoms.

The explanation is that while the salts are gathering in increasing quantities in the blood, the patient suffers from systemic poisoning, with all its nervous and constitutional phenomena, until certain unknown causes are called into operation and the poisonous salts are precipitated in the joints, relieving the blood of its poisonous contents and bringing about immediate improvement.

The physiologic chemistry of gout is far from clear. The disease must depend upon uric acid accumulation, because salts of uric acid form the gouty deposits, because there is a maximum of uric acid in the blood just before the occurrence of the gouty paroxysms, and because irregularities of uric acid excretion correspond with the paroxysms. The excretion of the uric acid is often continuously above the normal, so that we cannot but conclude that the disease depends upon increased production of uric acid rather than upon its retarded elimination.

The origin of the uric acid is obscure, but it is supposed that, like the other members of the alloxuric bodies, it results in part from the transformation of nuclein taken with the food, and in part from the metabolic processes of the body itself. Some think that proteid metabolism predisposes to it, because gout is common in those who take an excessive quantity of proteid food, and because of the chemical similarity of uric acid and urea. Others think it possible that sugars may have something to do with it, because in diabetes proteid destruction is accelerated by indulgence in carbohydrate foods.

As Lazarus-Barlow says, "The pathology of gout is bound up with questions as to the chemical combinations which uric acid can form in the body and the solubilities of these combinations."

Sir William Roberts, in discussing the relation of uric acid to gout, gives the following facts regarding its chemistry: Outside of the body uric acid can form with each of the alkalies a urate, a biurate, and a quadriurate. A urate can only be formed by the interaction of uric acid with sodium hydrate, potassium hydrate, ammonium hydrate, etc., and since these substances do not exist in the body, normal urates cannot enter into the question of gout. Nevertheless, it is usually said that the material in gouty joints is "sodium urate"; the deposit in uratic urine is a mixture of "sodium, potassium, and ammonium urates." The only salts with which we are concerned are the biurates and quadriurates. In the blood and in normal urine, uric acid only exists in the form of a quadriurate, a substance that is already sparingly soluble (1 in 500 of serum), that in an alkaline medium takes up another atom of base and passes into biurate, which is almost insoluble (1 in 10,000 of serum). The mortar-like substance in gouty joints is sodium biurate. Conditions, therefore, that affect the solubility of sodium biurate and its formation from the quadriurate are of great importance in considering the pathology of gout.

Though sodium biurate is only soluble to the extent of 1 part in 10,000 of serum, in pure water at 37° C. its solubility is about ten times as great. This difference in solubility apparently depends upon the presence of sodium salts in serum, for the solubility of the salt in water diminishes in proportion to the amount of sodium chlorid or bicarbonate in solution, so that, for example, in a 0.7 per cent. watery solution of sodium chlorid, sodium biurate is almost insoluble. Moreover, if the salt be removed from serum by dialysis, it dissolves as much biurate as does pure water. Hence, in the body deposition of sodium biurate will be more liable to take place according as the solution in which it finds itself contains more sodium salts.

But sodium biurate exists in two forms, a crystalline and anhydrous form (to which alone reference has hitherto been made), and a gelatinous and hydrated form that is very unstable and readily passes into the anhydrous crystalline form, but which is far more soluble in serum. In its passage to the crystalline biurate, sodium quadriurate passes through the hydrated variety of biurate, and the readiness with which this series of changes is carried out depends chiefly upon the amount of quadriurate present, and the presence or absence of sodium salts. The series of changes was found to take place more rapidly the higher the proportion of uric acid (*i. e.*, quadriurate) in solution. Thus, in Roberts's experiments, when uric acid was present in solution to the extent of 1 in 3000, precipitation of the biurate commenced on the third day; when present to the extent of 1 in 2000, precipitation commenced in thirty-three hours; when present to the extent of 1 in 1000, precipitation commenced in six hours. Similar experiments showed that the readiness with which crystalline biurate is precipitated from solutions originally containing quadriurate alone is hastened by the addition of sodium salts to the solvent, but is retarded by addition of potassium salts. At the temperature of the body, too, deposition of crystals occurs earlier than at the temperature of the room. As the result of all his experiments, Roberts concludes that an attack of arthritic gout can only take place when the synovia is impregnated with uric acid to the extent of about 1 in 2500. These facts indicate that an attack of gout occurs because the synovia and lymph are charged with quadriurate under conditions that lead to the precipitation of the crystalline biurate; the most important of these conditions being apparently high percentages of uric acid and of sodium salts in solution.

Oxaluria and Phosphaturia.—Among the chemical constituents of the urine whose excess or diminution is supposed to be indicative of erroneous metabolism, oxalic and phosphoric acids are to be regarded as important.

Oxalic acid occurs in normal urine, the total quantity excreted in twenty-four hours being about 20 milligrams. Its most usual combination is with lime, to form calcium oxalate. The presence and the number of the octahedral colorless crystals of this salt are usually taken as an indication of the quantity of the acid present, though such estimation is subject to marked error, because the precipitation of the salt in crystalline form depends upon a variety of conditions, the most important of which is the quantity of calcium in the urine. Of what significance oxalic acid may be is much disputed. Some hold that its presence depends solely upon its ingestion with vegetable foods, and that it has nothing whatever to do with metabolism, while others think it may be chemically derived from uric acid. The weight of opinion favors the view of accidental consumption in vegetable foods. An opinion that it depends upon deficient oxidation of carbohydrates is supported by the fact that the elimination of oxalic acid is increased in diabetes. The fact that marked increase of uric acid is usually associated with increase in the number of crystals of oxalate of calcium favors the relationship of the two substances. However, uric acid in excess usually occurs in markedly acid urine in which there is considerable disodic phosphate, which, by lessening the solvent power of the urine for the oxalates, makes them appear increased in quantity.

Some authors think the presence of oxalic acid in increased quantity is indicative of neurasthenia and other neuroses, but there is little evidence in favor of such a view.

The chief importance of oxalic acid attaches to the occasional formation of calculi (*q. v.*, calculi) when the urine is acid.

Phosphoric acid combined to form phosphates of magnesium, ammonium, and sodium is normally present in the urine, the total daily excretion amounting to 3.5 to 4 gm. When the urine is alkaline the salts precipitate, the most common crystalline form being the triple or ammoniomagnesic phosphate. The discovery of the precipitated crystals in the urine may not signify any marked increase in the total phosphoric acid, but simply an unusual precipitation and sedimentation. It is suggested by Stengel that the proper method of estimating and expressing phosphaturia would be by computing it in proportion to the nitrogen compounds, the normal ratio being 17 to 20 parts of phosphoric acid per 100 parts of nitrogen. When so computed it can be determined that real phosphaturia occurs, and that it is not dependent upon the diet, but upon errors of metabolism. Among the diseased conditions in which phosphaturia is marked may be mentioned diabetes mellitus, tuberculosis, and various bone diseases.

The occurrence of large phosphatic sediments in the urine is neither of clinical importance nor any real indication that the quantity of phosphoric acid excretion is increased.

Phosphatic salts frequently lead to calculus formation in the bladder and occasionally in the kidney. It occurs only when the urine is alkaline, as acidity keeps the salts in solution.

Perspiration is a means by which we rid our bodies of a considerable quantity of surplus water and of a certain proportion of solid excrementitious substances. By evaporation of the perspired water the temperature of the body is reduced.

Perspiration goes on all the time in a form known as *insensible perspiration*. At certain times and for certain reasons it increases in quantity, so as to become *sensible perspiration*. The average daily quantity for an adult human being in good health is 700 to 900 gm. This quantity is not to be looked upon as fixed, however, as when the external temperature is high, when much work is done and the temperature of the body elevated, when much fluid has been drunk, and when drugs of diaphoretic action have been taken, the quantity may greatly increase without becoming abnormal.

The chemical composition of the sweat is given in round numbers by Kirk as:

Water	98.88	per cent.
Solids	1.12	"
Salts	0.57	"
NaCl	0.22–0.33	"
Other salts	0.18	"
Fats	0.41	"
Epithelium	0.17	"
Urea	0.08	"

It will be observed that the constituents of the sweat are about the same as those of the urine, but that their proportions vary greatly. The fat and epithelium are derived from the skin and from its sebum.

I. The **perspiration may be diminished** (anhidrosis). In fever and after the administration of certain drugs (aconite and morphia) the insensible perspiration becomes considerably reduced as a part of general glandular inactivity, so that the skin becomes hot and burning to the touch. When the perspiration is diminished or checked, as by varnishing the skin, human beings suffer no inconvenience if the kidneys are normal. The lower animals fall into a cachectic condition if varnished, but this probably depends upon loss of heat regulation rather than upon loss of sweat.

II. The **perspiration may be increased** (hyperhidrosis) by the consumption of large quantities of fluid, by elevation of the surrounding temperature, and by the administration of such drugs as pilocarpin, calabar bean, strychnin, picrotoxin, muscarin, nicotin, camphor, and ammonia.

Nervous influences, such as shock, emotion, stimulation of the sympathetic nerves, etc., increase it. The elimination of micro-organismal poisons may take place partly by the sweat, so that the crisis of fevers is nearly always accompanied by profuse sweating.

Hyperhidrosis may occur from excessive weakness and collapse. The night sweats of phthisis probably depend upon the former condition.

III. The **perspiration may be peculiar in quality,** as in *chromidrosis*, a rare condition in which the sweat is dark colored, being sometimes bluish, blackish, reddish, greenish, or yellowish. This affection is said to occur most frequently in hysteric girls, and usually affects the face. It is associated with chronic constipation, and depends upon the elimination of *indican* in the perspiration.

Hematidrosis, or red sweat, also sometimes occurs from the entrance of blood into the sweat glands, or from the growth of colored bacteria in the secretion. *Bromidrosis* or *osmidrosis* usually follows local excessive sweating, particularly of the feet. It is characterized by a disgusting odor that results from the presence of specific bacteria in the secretion.

Irregular distribution of the perspiratory function, by which certain areas of the skin secrete actively while others reamin dry, usually depends upon irregularities of the sympathetic innervation.

Sympathetic Relationship Existing between the Perspiration and Urinary Secretion.—There is a distinct co-ordinated and sympathetic action between the secretions of the kidneys and the skin. This is well shown by the physiologic balance maintained under natural conditions. When the skin is active the kidneys secrete less; when the kidneys are active the skin is dry. The two functions are, however, not interchangeable, as the 0.04 per cent. of urea in the sweat can never compensate for the loss of the 2 per cent. excreted in the urine by the kidneys.

Bile.—The bile is a combined secretion and excretion of which the liver produces from 500 to 1000 c.c. daily. It leaves the liver in the form of a thin, watery, golden-red fluid, and is poured into the duodenum. The bile that collects by regurgitation in the gall-bladder is changed in quality and becomes much thicker, probably from loss of water by absorption, and contains mucus derived from the epithelium of the lining membrane.

The function of the bile is not thoroughly understood. Its retention is highly prejudicial to health, bringing about the condition known as icterus or jaundice. Its loss through fistulæ interferes with the digestion of fats and leads to constipation, though health is not seriously impaired.

The secretion of bile goes on continuously, but is subject to fluctuations depending upon the influence of food. As soon as chyme passes from the stomach into the duodenum the secretion of bile is at once greatly augmented, as if for some function subserved in connection with digestion. As the food passes on, it gradually declines until the absorption of food becomes active and the portal blood ascending to the liver becomes rich in the products of digestion, when it shows a second marked increase.

The bile is alkaline in reaction, and mixing with the acid chyme changes its reaction to alkaline, so that the pancreatic enzymes are able to operate. The composition of bile leads us to believe, however, that it has more useful purposes to perform than simple alkalinizing of the intestinal contents. It contains no enzymes of its own that have thus far been isolated, and seems devoid of any digestive action. Its composition is, according to Hammarsten:

Bile salts	9.14
Cholesterin, lecithin, and fat	1.18
Mucinoid material Pigment,	2.98
Inorganic salts	0.78
Water	85.92

	I.	II.
Water	97.48	97.160
Mucin and pigments	0.529	0.910
Bile salts	0.931	0.814
Taurocholate	0.3034	0.053
Glycocholate	0.6276	0.761
Fatty acid from soaps	0.123	0.024
Cholesterin	0.063	0.096
Lecithin Fat	0.022	0.128
Soluble salts	0.8070	0.8051
Insoluble salts	0.025	0.0411

The **bile salts** consist of the glycocholate and taurocholate of sodium, and salts of amido-acids, the latter containing sulphur. The importance of these salts, or rather of the acids of which they are formed, is not known. They do not exist elsewhere in the body, hence must be metabollic products of the liver cells. They are not excrementitious matter, as they do not appear in the feces. The salts are decomposed in the intestine into cholalic acid, taurin, and glycocin, small quantities of which appear in the feces; but it is estimated that seven-eighths of these substances are reabsorbed from the intestine, taken to the liver in the portal blood, and there resynthetized into bile salts again. When present in the blood the bile salts are poisonous and cause a marked bradycardia. They are readily absorbed in cases of ligature or calculous obstruction of the biliary ducts; but in cases of removal of the liver they are absent, evidently because they are not formed elsewhere than in that viscus. The synthesis of these salts in the liver cells, their analysis in the intestine, and their absorption from the latter to be taken back to the liver again, constitute what Schiff has described as the "bile circulation," and confirms the view that the salts and acids are important. It is discovered that when bile salts are experimentally introduced into the body the secretion of bile is increased, and it has been suggested that the use of the acids is to exert a regulating effect upon the liver function. The liver is so amply provided with nervous regulating mechanism, that this can scarcely be the sole office or even an important office of the acids.

The **bile pigments** (bilirubin and biliverdin) are derived from the blood. It is supposed that the hemoglobin liberated in the course of natural hemolysis is carried to the liver and there transformed to bilirubin and discharged into the bile as a waste product. In this process of transformation the iron is retained in the liver, to be used over again in the synthesis of new hemoglobin in the hematopoietic organs. Bilirubin readily takes up oxygen and is so transformed to *biliverdin*, a green pigment common in the bile of herbivorous animals. Bilirubin is golden in color and occurs in carnivorous animals. Neither bilirubin nor biliverdin occurs in the feces, as before reaching the rectum they undergo reduction to *hydrobilirubin*, or *stercobilin* the pigment of the feces. Probably considerable of the biliary pigments are reabsorbed from the intestine with the portal blood, to return in part to the liver for reelimination and in part to be excreted by the kidneys as *urobilin*, the coloring-matter of the urine.

Cholesterin occurs in the body in limited quantities in the nervous tissues. Although in some particulars bearing suggestive resemblances to fats, and for many years attributed to erroneous treatment of fats, by which its excessive occurrence was supposed to be amply explained, cholesterin is an alcohol, the source of which has not been determined. It is now believed to be derived from the nervous tissues and is commonly regarded as an excretion. Its small amount in liver bile is in marked contrast to the large quantity in the gall-bladder bile, and has led to the opinion that in the latter situation it is manufactured by the epithelial cells of the bladder wall.

Its chief pathologic interest is in the fact that when certain abnormal conditions arise, its precipitation from the bile is apt to be succeeded by the formation of calculi. (See Gall-stones.)

Lecithin is also a constituent of the bile, though present in small quantities only. It is supposed to be a waste product of the nervous system.

Nucleo-albumin.—The viscidity of bile depends entirely upon the presence of nucleo-albumin, not as was formerly thought, upon mucin. This substance is formed in the ducts. Traces of mucin occur in the bile.

So far as we are able at present to determine, therefore, the large quantity of bile poured every day into the intestine carries with it a very small quantity of cholesterin and lecithin that are discharged from the body as final waste products, certain salts that are decomposed, the acids being reabsorbed for further use, and certain pigments that are transformed to be reabsorbed in part and in part (hydrobilirubin) eliminated. Its alkaline reaction facilitates pancreatic digestion, and its combinations with fatty acids have something to do with the emulsification and absorption of fats.

The liver does more than secrete bile, but the products of its other activities (urea and glycogen) leave it in the blood, not in the bile. The bile contains no appreciable quantities of urea, and though formed, in all probability, in the liver, the urea is excreted by the kidneys.

Jaundice or **icterus** is a yellow or greenish discoloration of the skin and certain of the tissues caused by the presence of bile in the blood. When caused by complete obstruction of the biliary ducts the condition is accompanied by changes in intestinal digestion resulting from the lack of bile in that viscus, and changes in other organs to which the bile absorbed has been carried by the blood.

Jaundice was formerly divided into *obstructive* and *non-obstructive* forms. The explanation of obstructive jaundice is evident in cases of catarrhal inflammation of the ducts with swelling of the mucous membrane, obstruction by lodged calculi, and the growth of neoplasms. The non-obstructive forms were supposed to depend upon non-elimination of bile pigments preformed in the blood by the liver.

More recent writers have been accustomed to speak of *hepatogenous* and *hematogenous jaundice*, the former depending upon the absorption of formed bile from the liver or biliary ducts into the blood, either because the ducts were obstructed or the bile formed in excess. The hematogenous form, corresponding to the jaundice of non-elimination, occurs in conditions in which no microscopic obstructive lesion occurs to explain it. It is found in various infections and intoxications, among which may be mentioned acute yellow atrophy of the liver, yellow fever, malarial fevers, pyemia, scarlatina, typhus, and other infectious diseases, and in phosphorus, arseniuretted hydrogen, toluylendiamin, venom, and other poisonings, and occasionally as the result of severe emotions and injury (concussion) of the brain.

As in all of the conditions named, as well as in newborn infants, in whom jaundice (*icterus neonatorum*) is very common, active destruction of erythrocytes is in progress, it is logical to suppose that it depends upon the hemolysis. The liberated blood pigment is transformed into bile pigment and stains the tissues. It was formerly supposed that the transformation of hemoglobin to bile pigment occurred in the blood, but there can be no doubt that this is an error, as Minkowski and Naunyn have shown that when the liver is removed from geese and ducks, poisoning by arseniuretted hydrogen fails to occasion jaundice. In these cases, though hemoglobin is always present in the urine, bilirubin is always absent. The liver, therefore, is responsible for all forms of jaundice, and it is not improbable that all forms are not only hepatogenous, but that all forms are obstructive, for Afanassiew found that the destruction of blood corpuscles, leading to an excessive formation of bile pigments, occasions an abnormal viscosity of the bile that hinders its ready escape from the liver; and W. Hunter found that the concentration of the bile was associated with an extensive catarrh of the bile ducts in cases of jaundice resulting from the subcutaneous injection of toluylendiamin.

One important chemical difference existing between obstructive and non-obstructive and hepatogenous and hematogenous jaundice, so-called, is that in the former bradycardia is present, while in the latter it is absent. Physiologic experiments have, however, failed to explain why this symptom should be present in the one form and not in the other, for the bile salts that are responsible for the symptom must be present in the blood in both forms, and can, in fact, be discovered in the urine in both, though it has usually been stated that they are present in the urine only in obstructive jaundice.

The difference, therefore, is probably largely a quantitative one, by which in obstructive jaundice from calculi or neoplasms considerable quantities of the bile salts are absorbed, as compared with the cases without much obstruction.

The bile is absorbed by the lymphatics and thrown into the circulation after their circuitous course, or at once enters the capillary blood vessels of the liver from the overdistended and rupturing bile capillaries.

I. **Results of Absorption of Bile.**—The absorbed bile stains the majority of the tissues with which it comes in contact. The skin at first has a yellowish tinge, but in cases of protracted duration the oxidation of the pigment causes it to become greenish yellow, olive, or grayish green. The conjunctiva, because of its whiteness, is sometimes the first tissue to show the color. The subcutaneous fat, the serous membranes and their contained fluids, the vitreous humor of the eye, the lungs, and the kidneys also show the color, and the mucous membranes are also tinged. Of the excretions, the urine shows it first, then the sweat. Purulent discharges are also colored. The tissue of the nervous system is, however, normal in color, and the saliva, tears, and the gastric and pancreatic juices may be free of it. The liver is not always discolored in jaundice.

The absorbed bile not infrequently causes irritation of the peripheral nerve-endings, with the result that there is intense itching of the skin. The vitreous humor being stained, the patient, of course, "sees yellow" (*xanthopsia*).

Not infrequently in acute jaundice the pulse is found reduced in frequency (*bradycardia*) and may fall to 50 beats per minute, and in severe cases even to 20 beats per minute.

Fever, syncope, delirium, coma, and convulsions, if associated with jaundice, depend upon other causes.

II. **Effect of Loss of Bile upon Digestion.**—In cases of obstructive jaundice, or of biliary fistula, when the bile being diverted from its proper channels is lost, the effect upon intestinal digestion is soon shown by the presence of an excessive quantity of fat in the stools. The feces become altered in color from the absence of hydrobilirubin, and resemble potters' clay in color and quality. They may also be quite offensive in odor. The fat content of the feces greatly exceeds the normal, which seems to prove that the bile has an important digestive effect upon fats. It must, however, be remembered that in catarrhal jaundice and in calculi impacted in the duodenal papillæ the pancreatic duct may also be obstructed, and the lipolytic pancreatic enzyme also be deficient.

Jaundice soon disappears when its cause is removed. *Icterus neonatorum* is probably the most persistent form of acute jaundice, sometimes lasting for several months. This may depend upon the crystallization of the pigment in the tissues which makes its removal more difficult.

Feces.—The feces are composed of remnants and waste products. Physically they are brown in color and plastic in consistence, though quite variable in this particular according to the "habit" of each individual and his preference for considerable animal or vegetable food. The quantity passed each day averages about 200 to 500 gm., according as the diet is chiefly nutritious (proteid) or innutritious (vegetable). They have a characteristic odor, chiefly dependent upon *skatol* and *indol*. They usually contain considerable putrefactive gas, that causes them to float in water.

Microscopically they consist of bits of undigested and indigestible animal foods, scraps of vegetable cells, with considerable cellulose, starch granules, globules of fat, and bacteria.

Chemically they contain the products of bacterial energy, *excretin*, a crystallizable non-nitrogenous substance, present in small amounts, cholesterin, probably derived from the bile, and from vegetable foods, mucus, fats, hydrobilirubin, and inorganic salts.

Probably the most important elements in the feces, so far as their effect upon the health of the individual is concerned, are the bacteria and their products. Of the bacteria there are many forms, the most constant being Bacillus coli communis in the adult and Bacillus lactis aërogenes in the infant. It is upon the presence of these bacteria and the decomposition and fermentation of the food that they occasion that the occurrence of skatol and indol depends.

Unfortunately very little is known concerning the bacterial products, and we are unfamiliar with the effects produced by their absorption. Very likely their importance is being greatly overestimated, as a certain proportion of the indol and skatol is constantly absorbed, forming the indoxyl-sulphuric acid and skatoxyl-sulphuric acid that occur in the urine. When much of these substances is absorbed from the intestine, correspondingly more appears in the urine; but the importance attributed to the presence of indican in the urine a few years ago has now greatly declined.

Concerning the autointoxication that occurs from the feces, we cannot fail to observe cases in which the feces are discharged only at weekly, monthly, or much longer intervals, yet without poisoning the patient.

Diarrhea is a condition in which the bowel movements are too frequent and the feces too soft.

It may depend upon a great many causes, all of which operate in one of four ways: 1. Increased rapidity of peristalsis, by which the feces are hurried along in an unfinished condition. 2. Increased secretion by the intestinal glands, by which the contents are kept too fluid. 3. Diminished absorption of fluid in the large intestine, by which the feces are not dried as usual. 4. Excitation of the nervous regulations affecting peristalsis and secretion.

Probably the greater number of diarrheas depend upon combinations of these causes, and it may be impossible to determine which is the chief factor. Thus, irritating substances, such as croton oil, by their local action upon the mucous membrane produce stimulation that causes accelerated peristaltic action and at the same time increases secretion. They may also excite the nervous mechanism, and by the increased peristalsis certainly effect the discharge of the intestinal contents before they have been dried and formed.

Diarrheas are divided into many groups according to various conditions under which they occur, as shown in the following table:

PRIMARY DIARRHEA:			
	ACUTE	Mechanical.	Irritative.
			Lienteric.
			Crapulous.
		Inflammatory.	Catarrhal.
			Infantile.
			Serous.
			Gelatinous.
			Mucous.
		Infectious.	Tropical.
			Choleraic.
			Choleriform.
			Dysenteric.
			Fibrinous.
		Obstructive—Pseudodiarrhea.	
	CHRONIC	Obstructive—Chylous.	
		Hepatic and pancreatic—Fatty.	
		Infectious—Tropical.	
SECONDARY DIARRHEA:			
	CHRONIC	Symptomatic.	
		Cachectic.	
		Vicarious or compensatory.	
		Nervous.	

Constipation or *coprostasis* is habitual insufficient movement of the bowels and is usually associated with hardness and dryness of the feces. The condition is largely one of individual "habit," some persons suffering from a mild degree of it all their lives. The average normal human being has a bowel movement every day, but the maintenance of health does not require this. Some persons have movements every other day, or every third day. A few persons have regular movements weekly. Cases are recorded in which the bowels moved only at intervals of months, and one case is reported in which there was no movement for a year. Suddenly developed retention of fecal matter, such as we observe in intestinal obstruction, is followed by serious symptoms (nausea, vomiting, stercoraceous vomiting, prostration, and exhaustion) never seen in habitual constipation, probably because in the latter we gradually become immunized to the products of bacterial putrefaction and chemical change absorbed from the intestine. The amount of damage the absorption of these products may occasion is not known. Sir Andrew

Clarke thought them capable of causing anemia, and described chlorosis as depending upon "*copremia*" or absorption of fecal products.

The causes of constipation are probably numerous. Diet has much to do with it, an innutritious diet by the amount of residual substance predisposing to frequent movements. There are, however, many persons who are not influenced in the least by alterations in diet, or are only temporarily influenced by it. Inertia of the bowel may be an important factor. If peristalsis is slow the feces are delayed in passage and become overdried, their further passage being delayed by their increased consistency. The rapid absorption of water from the chyme after it enters the large intestine causes the feces to dry prematurely, so that very often small rounded masses (*scybala*) are formed and pack together in irregular masses that pass on with difficulty. Failure of the nervous mechanism of the intestine properly to innervate the organ may delay peristalsis and produce premature drying and difficult progress of the feces. Obstruction of the lumen of the organ by intussusception, volvulus, hernia, neoplasms, fibrous adhesions between viscera, structures, etc., all bring about acute or chronic constipation according to the condition and its duration. An analysis of the causes given by Lazarus-Barlow finds them all depending upon: 1. Obstruction. 2. Impairment of the intestinal propulsive power. 3. Abnormal consistency of the feces. 4. Lowered reflex irritability of the defecation center in the lumbar cord.

Obstruction of the bowels with complete retention of the feces (obstipation) is a much more mischievous trouble. It may be acute, depending upon peritonitis, general or local as in appendicitis, hernia, intussusception, volvulus, foreign bodies, etc., or it may be chronic and follow prolonged increasing constipation in cases of stricture of the bowel, neoplasms, and fibrous adhesions.

In *acute obstruction* the bowel is completely closed to the passage of fecal matter at some point at which the disease is situated. Below this point the irritation of the injured or diseased tissue may hurry the bowel to empty its contents (spurious diarrhea). When once emptied the bowel ceases to act. The patient usually becomes profoundly shocked, is prostrated, becomes nauseated, and vomits. The vomitus is at first gastric contents, followed shortly by bilious matter and later by fecal matter (stercoraceous vomiting). The urine is usually diminished in amount. The patient becomes collapsed, and dies exhausted in from five to seven days.

Stercoraceous or fecal vomiting seems to depend upon the activity of the peristalsis that, driving the semi-fluid intestinal contents toward the obstruction, which it is unable to pass, brings about a returning ascending stream in the center of the bowel. It is from this returning stream that the vomited fecal matter is derived. The patient is, of course, unable to nourish himself under the circumstances, and the lack of nourishment, the prostration, and the collapse combine to hasten the fatal outcome.

Chronic obstruction occurs in cases of gradually forming neoplasm, of slowly contracting strictures and peritoneal adhesions, slowly impacting fecal matter, etc. In it the long preceding period of constipation paves the way to a tolerance of the absorbed fecal products. During the time fecal matter is accumulating in quantity in the bowel, the patient suffers from gradually increasing headache, foul tongue, bad breath, impaired intellect, and abdominal distention. Foul eructations, occasional vomiting, sometimes fecal in character, may be observed. Ultimately the termination is fatal.

As Lazarus-Barlow points out, it is extremely difficult to understand why acute obstruction should be so dangerous and rapidly fatal, and chronic obstruction so different. He looks upon the shock and peritonitis as being of great importance. Very probably there is in chronic obstruction as in chronic constipation the development of a vicarious eliminative channel for absorbed products, as well as the development of immunity to the effects of fecal absorption, neither of which conditions has time to occur in acute obstruction.

End-products.—The fulfilment of the nutritive function gives rise to final or end-products which, being of no further use, are discharged from the body.

The undigested and indigestible residuum of the food forms the bulk of the feces and is discharged from the rectum.

The fats and carbohydrates of the food are split up to CO_2 and H_2O, the CO_2 being chiefly eliminated by the lungs. The proteid foods after having performed their function are transformed in the liver to urea, in which form they are excreted by the kidneys. The salts consumed by the foods and absorbed into the blood also find excretion in the urine. The nucleic acid taken in the food is transformed to uric acid and, together with oxalic acid in the form of oxalates, and kreatinin derived from the kreatin of the muscle, are eliminated in the urine. Cholesterin, possibly derived from nervous-tissue waste, passes out with the bile and escapes with the feces. Leucin, tyrosin, lecithin, and stercorin, as a rule, escape as fecal constituents. Leucin and tyrosin sometimes pass out with the urine. Cystin of obscure origin is found in the urine. The waste blood pigment forms the coloring-matter of the bile, and, being transformed in the intestine, is in part used over again, in part absorbed to form the urobilin that colors the urine, while the remainder escapes as the hydrobilirubin that is the natural pigment of the feces.

CHAPTER IV.

PATHOLOGY OF THE CIRCULATION.

The cells of the body derive their nourishment from a circulating nutritious fluid, the source of which is the blood. Alterations in its chemistry, changes in the regularity of its circulation, and irregularities in its distribution profoundly influence the health of the tissue elements.

ISCHEMIA.

Anemia, or general bloodlessness, finds its proper consideration under Diseases of the Blood.

Ischemia, or local anemia, is an insufficiency of blood in a part of the body.

Causes.—Ischemia may depend upon:

1. Abnormal contraction of the arteries, depending on vasomotor constriction, as in Raynaud's disease, ergot-poisoning, etc.
2. Compression of arterial vessels by morbid growths, etc.
3. Disease of the blood-vessel walls with diminution of their caliber, as in the chronic forms of endarteritis.
4. Thrombosis and embolism.
5. Ligature of a vessel, and compression of the tissues by an Esmarch tube.

Ischemia is rarely complete because of the numerous anastomoses of the arterial vessels, and for the same reason is seldom permanent, except when caused by extensively diseased vessels. Sudden complete ischemia is apt to be succeeded by *infarction* (*q. v.*), either anemic or hemorrhagic.

Morbid Anatomy.—During life an anemic part is pale in color, cool to the touch, and is without visible vessels upon the surface. Post mortem the organ appears unusually pale and bloodless, of a translucent appearance, has few visible blood vessels, and is dry when incised, no blood escaping from it.

Morbid Histology.—The histologic findings confirm the naked-eye appearances. The part appears empty of blood, and signs of secondary changes are evident.

Terminations.—Ischemia produces varying results according to its degree. Complete bloodlessness inevitably results in gangrene, infarction, or necrosis; incomplete bloodlessness in degenerations or atrophy. Temporary and very moderate ischemia may not produce noticeable changes.

HYPEREMIA.

Hyperemia is a condition in which the tissues receive an excess of blood. The blood is contained within the vessels, small quantities sometimes escaping from them. The condition may be *active* or arterial, or *passive* or venous. Capillary hyperemia may be either.

Active Hyperemia.—This condition is known as *acute congestion*; in it the tissues receive an excess of arterial blood. Two forms are known:

I. *Idiopathic hyperemia*, resulting from impairment of the resisting power of the arteries. Its causes are numerous, and are divisible into two classes.

(*a*) Causes acting directly upon the arterial vessels and producing in them a paralytic relaxation as traumatism, inflammation, extremes of temperature, physiologic action of certain drugs, pathologic conditions of the blood-vessels, etc.

(*b*) Causes operating through the nervous mechanism of the vessels by producing palsy of the vasoconstrictor nerves (neuroparalytic hyperemia) or by producing stimulation of the vasodilator nerves (neurotonic hyperemia).

II. *Collateral hyperemia*, in which a vessel receives an increased quantity of blood diverted from normal channels that have been obstructed. If the main trunk of an artery is obstructed, the pressure of the circulation is thrown upon its major branches and extends to their capillaries. The condition affects the larger vessels, but is most apparent in the capillaries.

Morbid Anatomy.—The congested organs are slightly increased in size because of the increased amount of blood that they contain and from an exudate escaping from them. They are bright red in color from the presence of arterial blood. The capillary redness appears as a diffuse scarlet blush. When larger vessels are turgescent they appear intensely red and unusually conspicuous to the naked eye; such prominent vessels are said to be injected. Capillary vessels can never be seen with the naked eye, no matter how engorged with blood they may be, so that this condition of injection always refers to the arterioles. The appearances change after death, the red color disappearing as the blood sediments to the dependent portions of the body.

The true nature of the blood found in the part after death may be difficult to determine. Its red color can only be taken to indicate arterial hyperemia when the organ appears bright red immediately after being incised. Redness at any later period may depend entirely upon the absorption of the oxygen in the air by the hemoglobin in the red corpuscles.

The redness of the skin occasioned by capillary dilatation, such as is seen in active hyperemia, is commonly described as *erythema*. Many varieties of erythema are described by dermatologists and others, but all depend upon the vascular dilatation. One of the most interesting and most important, probably depending upon disturbances of vaso-motor innervation, chiefly occurs in the tissues of the lower limbs and forearms, though occasionally in those of the upper arms and thighs. It is called *erythema nodosum*, and is characterized by sudden painful dilatation of the radicles of some single vessel, resulting in the formation of a somewhat painful, hard swelling varying in size from a pea to an orange, and sometimes situated in the subcutaneous, though occasionally in the muscular tissues. So soon as the disturbance of innervation is past the vessels return to their usual size and the pain and swelling disappear.

Results of Active Hyperemia.—Active hyperemia is followed by certain changes in the parts affected.

1. *Hypertrophy*. The hyperemic part becomes larger than normal, at first because it contains more blood than usual, and later the increased nutrition brought to it leads to multiplication of the cells.

2. *Parenchymatous degeneration*, probably resulting from overnutrition or excessive stimulation of the cells.

3. *Fibrosis*. This is particularly frequent as a consequence of collateral hyperemia, and is characterized by proliferation of the connective tissue immediately around the blood vessels, as if its development were intended to afford them additional support.

Passive Hyperemia.—Passive hyperemia is the presence of an excess of venous blood in a part from which its exit is obstructed. The blood pressure in the veins is very low and, indeed, in some large veins like the inferior vena cava is negative, the blood being driven out of them by the pressure of the blood entering from the capillary system, the pumping action of the muscular contractions and the respiratory movements. The occurrence of passive hyperemia is, therefore, a much more simple phenomenon than that of the active congestion.

Causes.—Passive hyperemia results from :

1. *Valvular heart disease.* Almost any obstructive or regurgitant disease of the heart brings about a secondary engorgement of the venous system, the strain of which is felt most severely upon the lungs, abdominal organs, and lower limbs.

2. *Cirrhosis of the liver*, interfering with the return of blood from the portal system, the engorgement occurring in the distribution of the portal vein.

3. *Compression and ligation of the veins*, preventing the exit of the blood and causing the venous elements of the tissue to become engorged. Such pressure is often unintentionally exerted upon the veins of the limbs by tight elastic garters. The dilated and tortuous veins from which the blood is prevented from escaping appearing upon the surface of the limb as the familiar varicose veins.

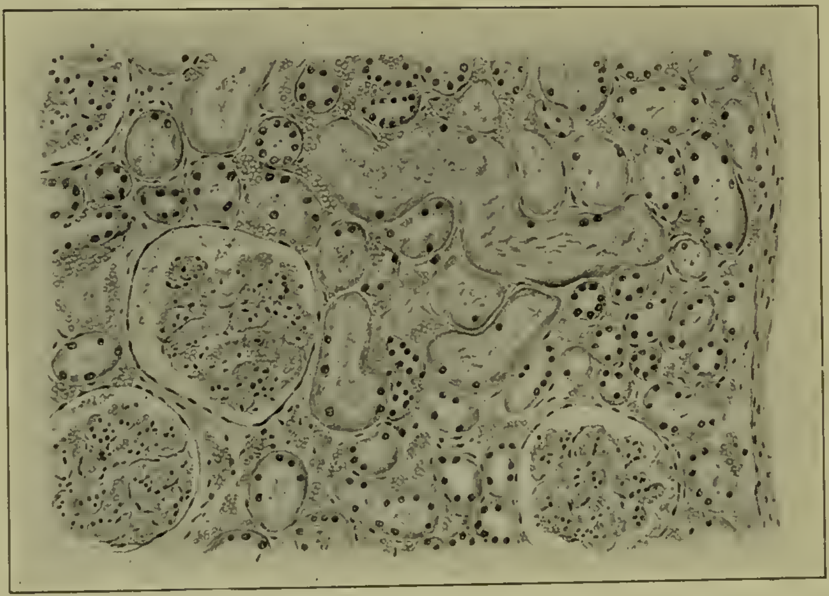

FIG. 33.—Passive hyperemia of the kidney. The capillaries and small vessels are everywhere distended with blood (Dürck).

4. *Obstruction of veins by thrombi.*

5. *The effect of gravity upon a weak circulation* and weak vessels (hypostatic congestion).

6. *Loss of vasomotor tone of the vessels.*

Morbid Anatomy.—In passive hyperemia the affected part is swollen and may be edematous. It has a dull grayish-blue or ashen color, and usually feels cooler than normal. When it has persisted for some time the vessel walls may yield to the gradually dilating force and appear in bluish streaks, or the larger superficial vessels may present marked varicosities. In prolonged passive congestion the tissues suffer from proliferative changes in the connective tissue, which undergoes hyperplasia both of fibrous and elastic elements. The presence of the dilated vessels and increased connective tissues frequently bring about atrophy of the more delicate tissues in parenchymatous organs, such as the kidneys, while the contraction of the newly formed connective tissue predisposes to subsequent reduction in size. An organ thus becomes small and feels hard as the result of chronic congestion (cyanotic induration).

Morbid Histology.—Under the microscope a turgescence of the veins and capillaries is detected.

Results of Passive Hyperemia.—The passive pressure opening the stigmata of the vessels very often allows red blood corpuscles to be squeezed through into the surrounding tissue (diapedesis). These blood corpuscles being subsequently destroyed, their pigment is liberated and often collects in and discolors the tissue, leading to cyanotic or *brown induration* or *brown atrophy*.

Passive congestion may also lead to edema, atrophy, degeneration, necrosis, and gangrene, according to its extent, degree, and duration. Perhaps the most frequent result of passive hyperemia is phlebectasia, or dilatation of the veins.

An interesting form of passive congestion depends upon *diminution of the atmospheric pressure*. A local form of this is seen in the application of dry cups to the skin, another in the sudden removal of fluid accumulations from the tunica vaginalis testis, pleura, etc. Universal turgescence of the venous system follows the rarefication of the air seen in high altitudes and in the pneumatic cabinet.

EDEMA OR DROPSY.

Edema is distension of the interstices of the tissues by clear watery fluid. A fluid closely resembling the plasma in composition, but usually more watery, constantly passes through the endothelial membranes, the capillaries, and supplies such metabolic tissue elements as are not in immediate contact with the capillaries with moisture and nutriment. This transuded fluid is known as lymph. Provision is made for its removal from the tissues after it has fulfilled its purpose through the lymphatic vessels, which begin as mere clefts and gradually develop into larger and larger vessels so as to provide a system of tissue drainage. There is a physiologic balance between the circulation of the blood and the lymph, so that no more fluid exudes into a tissue than it needs. In diseased conditions this balance is frequently disturbed, and the amount of transudate increased in such a way as to cause the tissue to become distended, saturated, macerated, and tumefied. This condition is known as *edema* or *dropsy*.

Causes.—Edema may result from :

I. *Increased transudation from the blood*, caused by

(*a*) *Hyperemia.* Active hyperemia causes edema because of the increased blood pressure and associated increased transudation. It more commonly occurs in passive hyperemia. Experiment shows, however, that hyperemia alone is insufficient to bring about dropsy. When the major vein of a healthy limb is ligated, causing intense passive hyperemia, edema does not occur unless the lymphatic trunk is also obstructed. Curiously enough, the results of experiment and disease seem to differ, for while it is a common experience in human medicine to find local edema following obstruction of the veins, as in thrombosis, after the vena cava of the dog is experimentally ligated, dropsy occurs only in that limb whose major nerve was severed, notwithstanding the extreme passive hyperemia that necessarily followed ligation of the vena cava. Obstruction of the lymphatic circulation also fails to produce dropsy.

(*b*) *Changes in the quality of the blood* may permit a greater amount of transudate than normal and so cause edema. Such hydremia is seen in disease of the kidney, where the retained water passes through the blood-vessel walls into the tissues. Here again experiments conflict with theory, for the researches of Cohnheim and Lichtheim show that when large quantities of water are injected into animals, so that hydremic plethora results, dropsy does not occur, the fluid being rapidly discharged by the kidneys, intestines, salivary glands, liver, and pancreas. At the same time a large amount of lymph is poured into the circulation through the thoracic duct, though the flow of fluid through the lymphatics of the limbs is not increased. These experiments seem to show that in addition to the increased water in the blood, some other factor is necessary. The experimenters quoted found that when venous hyperemia of one limb was added to the general hydremia that limb became dropsical.

(*c*) *Changes in the walls of the blood vessels.* Cohnheim taught that the most important change leading to dropsy is to be found in malnutrition of the blood-vessel walls.

(*d*) *Changes in the vascular innervation.* This is best illustrated by the angioneurotic local edemas occurring in consequence of dietetic errors.

(*e*) *Changes in the extravascular pressure*, as in edema ex vacuo already mentioned.

II. *Impeded removal of fluid from the tissues* because of obstruction or inefficient action of the veins and lymphatics.

(*a*) *Obstruction of the lymphatics* is rarely followed by dropsy. Experimentally it is not possible to produce edema by the most thorough ligation of the lymphatics of the limb, and even ligature of the thoracic duct, which must be followed by an engorgement of the entire lymphatic system, is by no means regularly followed by dropsy, probably because of the frequent anastomoses between the veins and lymphatics.

(*b*) *Obstruction of the veins* is one of the most important mechanical causes of dropsy, though it has already been pointed out that experiments upon dogs differ upon this point from disease in man. The difference may be attributed to the more healthy condition of the tissues of the experiment animal. In cases of carcinoma of the breast with secondary disease of the axillary lymphatic glands, edema of the arm is frequent, presumably from obstruction of the lymphatic circulation; but usually in these cases no examination is made to determine whether disease of the nerves or veins is added to the lymphatic obstruction.

Edema thus seems to depend upon a combination of causes in most cases rather than upon some one in particular. The chief *clinical causes* are cardiac insufficiency, causing edema that first appears in the feet and ankles; kidney disease, appearing first about the eyes and face; anemia and cachexia; cirrhosis of the liver, affecting the abdominal cavity; and pressure upon the veins or lymphatics from a gravid uterus, abdominal or other neoplasms, etc.

Chemistry.—The dropsical effusion is a clear, straw-colored, sometimes slightly blood-stained, albuminous fluid. The amount of proteid is usually less than 3 per cent.; therefore, much less than that of the liquor sanguinis and less than that of inflammatory exudates. It does not contain fibrin, as a rule, though a small quantity may be present. The liquid usually coagulates upon the addition of a fibrin ferment, showing that it contains fibrin factors. Fluids from dropsy of the pleura are most rich in proteids; subcutaneous effusions least so. The specific gravity of the fluids in dropsy averages about 1.015.

Special Forms.—*Anasarca* is universal edema of the subcutaneous tissue. It usually results from diseases of the kidneys. The whole body appears swollen, especially where the tissues are loose. The skin is very white and smooth, usually feels cool, and when pressed upon yields readily, leaving a pit or depression when the finger is removed.

Ascites is dropsy of the peritoneal cavity. Instead of being in the interstices of the areolar tissue, the fluid is free in the cavity of the abdomen. It results from cirrhosis of the liver, malignant disease of the abdominal viscera, venous obstructions, etc.

Hydropericardium is a collection of fluid in the pericardial sac. This is usually inflammatory in origin, and rarely a simple dropsical effusion.

Hydrothorax is a collection of fluid in the pleural cavities. It is common as a part of general dropsy, but more common as the result of enfeebled cardiac action. It is nearly always bilateral. When unilateral it usually occurs on the right side, and has been thought to depend upon circulatory disturbances resulting from the pressure of an overdistended right auricle upon the azygos and other contiguous veins.

Hydrocephalus is an accumulation of fluid in the ventricles of the brain; it is probably of inflammatory origin. Two forms are described: *external hydrocephalus*, in which the fluid is in the subarachnoidean space, and *internal hydrocephalus*, in which it occupies the ventricular cavities.

Hydrocele is an accumulation of fluid in the tunica vaginalis testis. It also applies to fluid collections about the cord and round ligament, and is occasionally applied to other fluid collections.

Pathologic Histology.—The *histology of edema* is very simple, the component elements of the affected tissue appearing to be more widely separated from one another than usual. In many cases the cells show a dropsical condition and appear vacuolated from imbibition of fluid.

EMPHYSEMA.

Interstitial emphysema is distention of the cellular tissue by gas. The condition is rare, and depends upon the accidental entrance of air from the surface of the body or from the respiratory apparatus, or upon the production of gas in the tissues by bacteria. It is seen chiefly in traumatic injuries of the chest. The affected area is swollen, pale in color, and crackles under the finger when pressed upon.

The gases produced by bacteria may be formed during the life of the animal, as in malignant edema and "black leg" or "quarter evil," or, as is probably more frequent, after death, as in infection with the Bacillus aërogenes capsulatus. In the latter gas bubbles (gas cysts) are found scattered throughout the organs, and are easily recognized in the brain, kidneys, and other solid organs.

HEMORRHAGE.

By hemorrhage is understood the escape of all the constituents of the blood from the heart or vessels. Three kinds of hemorrhage are described: the *arterial*, the *venous*, and the *capillary*. Hemorrhage occurs by *rhexis* or rupture of the vessel wall, or by *diapedesis*, in which there is no discoverable laceration of the walls of the vessel. Just how the corpuscles pass out of the vessels in diapedesis is not well understood. It is commonly understood that the corpuscles escape through the stigmata of the vessel walls, which, on account of hyperemic distention, are abnormally stretched and permit both the fluid and the corpuscles to escape. The possibility of minute lacerations of the vessels being present but not discovered must always be borne in mind.

Hemorrhage by Rhexis.—**Causes.**—1. *Increased blood pressure*, especially when, because of disease, the vessel walls have lost their elasticity or supply aneurysmal dilatation.

2. *Disease of the vessels.* In atheroma, calcification of the coats of the arteries, aneurysms, and fatty degeneration of the vessels their walls may be unable to stand the normal blood pressure, and yield with resulting hemorrhage. Increased blood pressure following exertion is usually the exciting cause.

3. *Traumatism.* This is the most frequent cause of hemorrhage and needs no further discussion.

By surgeons hemorrhages are divided into *primary* or immediate and *secondary* or recurrent: primary hemorrhage immediately following the solution of the continuity of the vessels walls; secondary hemorrhage resulting some time after the original injury, from sloughing of the tissues or from the separation of a ligature.

Hemorrhage by Diapedesis.—Causes.—1. *Certain diathetic diseases,* such as scurvy, purpura hæmorrhagica, various of the exanthematous diseases, hemophilia, pernicious anemia, and leukemia. In all of these malnutrition of the vessel walls together with minute lacerations may be found.

2. *Inflammation.*—In nearly all violent inflammations erythrocytes as well as leukocytes escape from the vessels; but here again lesions of the vessels sufficient to explain the hemorrhage occur. Croupous pneumonia is an inflammatory condition in which, however, it may be difficult to find vascular lesions sufficient to account for the extensive hemorrhagic exudate.

3. *Hyperemia.*—In extreme hyperemia, both active and passive, some erythrocytes escape from the vessels.

4. *Intoxications* of various forms may lead to hemorrhagic extravasations, but in those in which they are most marked, as in venom-poisoning, there are distinct lesions of the vessel walls.

5. *Alterations of Innervation.*—These probably explain the peculiar cases of vicarious menstruation occasionally seen, as well as the hysteric stigmata.

6. *Hemophilia.*—In this affection the bleeding is more rarely spontaneous, however, than dependent upon slight traumatic injuries of the vessels.

Special names are applied to hemorrhages from or into certain parts: *Epistaxis* is hemorrhage from the nose; *hematemesis,* from the stomach; *hemoptysis,* from the lungs; *hematuria,* from the urinary organs; *menorrhagia* or *metrorrhagia,* from the uterus; *melana* or *enterorrhagia,* from the bowels; *hematothorax,* into the pleural cavity; *hematocele,* into the tunica vaginalis testis; *hematidrosis,* in the perspiration, etc.

Special Forms of Hemorrhage.—1. *Petechiæ.*—These are minute circumscribed subcutaneous, submucous, and subserous hemorrhages, varying in size from a pin-head to a pea. They usually occur in specific fevers and the disease known as purpura hæmorrhagica.

2. *Ecchymoses* are larger, and are familiar as the discolored areas known as bruises. The terms *suffusion, extravasation,* and *sugillation* are applied to large areas of this kind.

3. *Hematoma* is a collection of blood in a solid tissue. Hematomata are often found upon the ears of insane persons (*hematoma auris*), and were once supposed to occur spontaneously, but are now known to result from traumatism. A variety of hematoma occurring on that part of the fetal head which presents for a considerable time at the os uteri in difficult labors is called *cephalohematoma.* The lesion is usually unilateral. When the blood beneath the pericranium elevates it, a ring of bone is usually found about the hematoma, and a layer of bone sometimes over it.

4. *Hemorrhagic Infarction.*—This is saturation of a circumscribed tissue area with blood that exudes from the vessels in consequence of obstruction.

Hemorrhage into the Tissues.—The blood that escapes from the vessels in hemorrhage always flows in the direction of least resistance, usually from the body, sometimes into the cavities of the body. Occasionally it saturates the loose tissues, filling all their interstices. The blood mass, especially when large, by coagulating in its spaces and interfering with its circulation, destroys the tissue and devitalizes it. Experience indicates that tissues saturated with blood are more than others predisposed to infection. The escaped blood undergoes the peculiar phenomenon known as coagulation, in which fibrin factors contained within it uniting with fibrin ferments, probably derived in part from external sources, lead to the formation of fibrin, a new and solid substance. The formation of fibrin in the tissue greatly retards the absorption of the clot and the restitution of the tissue.

The resorption of escaped blood is by no means a simple process. First the serum is taken up by the lymphatics; then the corpuscular mass that remains slowly disintegrates, the hemoglobin being set free and changed to hemosiderin, granules of which are found scattered through the tissues. These are removed slowly on account of their insoluble nature, phagocytic cells playing an important part in the process.

Ultimately the pigment seems to find its way into the urine, by which it is eliminated. If the coagulation of the blood within the tissue has produced a profound disturbance, the changes already described must be followed by colliquation necrosis and absorption of the damaged elements of the tissue. Following such absorption a cyst not infrequently remains, especially in the brain. It contains clear fluid with a sediment of hematoidin crystals. Hemorrhages into serous cavities may be absorbed without coagulation and without infection.

Hemophilia.—In rare cases in which no distinct alterations of the structure of the vessels have been discovered a peculiar tendency to bleed upon very slight provocation is sometimes observed. This condition is described as *hemophilia*. From a trifling cut or scratch, persons affected with this disease have been known to bleed to death. Agnew saw a case in which the bleeding was always from injuries above the neck, never from any other part of the body. The disease is usually hereditary, and is usually transmitted through the daughters of the bleeder to their male descendants. One famous family of bleeders—the Appleton-Swain family, of Reading, Mass.—has been traced through seven generations. The disease affects the males chiefly, and usually develops before the tenth year. Persons in all walks of life are subject to it, and those affected are healthy in appearance and are said to have fine, soft skins.

Bleeding most frequently occurs from the nose, mouth, stomach, bowels, urethra, and lungs; sometimes from trifling cutaneous cuts and scratches. Sometimes the hemorrhage appears to depend upon diapedesis. The blood may persist in flowing for hours or even for days. The use of astringents and hemostatics is without avail, and ligation cannot be practised, lest the operation produce worse bleeding than was originally present. The disease is also characterized by an affection of the joints, closely resembling acute articular rheumatism. The nature of the disease is still uncertain. It seems to depend more upon interference with the coagulability of the blood than upon alteration in the blood vessels, although changes both in the blood and the vessels may be present.

Spontaneous Arrest of Hemorrhage.—Hemorrhage, no matter how severe or from however large a vessel, would eventually cease spontaneously should the escaping blood reduce the intravascular pressure to zero. As, however, this would necessitate that everyone with a severed artery must die, nature provides other methods of checking the outflow of blood from the vessel.

1. The injury that severs the vessels causes it immediately and forcibly to contract, the lumen of the vessel becoming much diminished in size. Again, the cut vessel being elastic retracts within the tissue so soon as it is divided, a smaller amount of blood thus escaping.

2. The blood coming into a new environment coagulates, first without, then upon, and finally within the vessel, forming a clot without and a coagulum, known as a *thrombus*, within. In this manner the vessel becomes completely plugged and the flow of blood stopped.

Results of Hemorrhage.—The result of hemorrhage will vary according to its extent. The loss of small quantities of blood is of no moment. Larger losses may be followed by fainting and unconsciousness, from which the patient finally recovers. Still larger losses cause unconsciousness with convulsions and doubtful recovery. Very large hemorrhages cause death from cerebral anemia. Repeated small hemorrhages are more serious than single large ones, though the general health of the animal has much to do with its effect. Healthy animals may be bled large quantities at frequent intervals, yet be able to regenerate the loss without apparent inconvenience. Thus, in animals immunized against bacterial toxins and bled to secure antitoxic serums, I have withdrawn one-tenth of the total blood bulk every week for months without appreciable change in the health of the animal. This will be further discussed in a future chapter (Diseases of the Blood).

LYMPHORRHAGIA.

Lymphorrhagia is the escape of lymph from the normal channels. It may depend upon traumatism or pathologic obstruction and rupture of the passages. In wounds of the neck the thoracic duct, if severed, frequently forms an external fistula, from which the chyle flows, the loss of the chyle ultimately causing emaciation and death.

Obstruction or disease of the thoracic duct within the chest, by permitting the escape of chyle into the pleural cavity, leads to *chylothorax;* into the abdominal cavity, to *chylous ascites.* The obstruction of smaller lymphatic vessels, as by filaria or other parasites, may cause *chyluria*, *lymph scrotum*, and *elephantiasis.*

THROMBOSIS.

By thrombosis is understood the coagulation of the blood within the vessels during life. It is really coagulation necrosis of a portion of the blood. In the process of coagulation the blood changes from a fluid to a solid by the formation of a new substance known as fibrin. Fibrin is not originally existent in the blood as such, but occurs in the blood in the form of soluble fibrin factors, prone to unite with the formation of insoluble fibrin the moment proper conditions are brought about.

When the blood clots outside the vessels, the resulting mass is known as a *coagulum* or *clot.* When it clots inside the vessels, the resulting mass is spoken of as a *coagulum* if it forms after death, or a *thrombus* if it forms during life.

Etiology.—During health the moving blood meets with no other surfaces in its circulation than those of the smooth endothelium of its vessels. It is a law of physiology that when normal blood passes with normal rapidity through normal vessels coagulation cannot take place. In diseased states any of these three conditions may be destroyed, so that thrombosis may result from changes in the blood, changes in the vessel, or changes in the rate of circulation.

1. **Changes in the Blood.**—(*a*) The accidental or experimental introduction of certain chemical and physical substances into the blood, by injuring the corpuscles and so liberating the fibrin ferments, may occasion thrombosis. Among the substances capable of doing this are alcohol, ether and chloroform, thymus extract, and heterogeneous blood serums.

(*b*) The occasional accidental entrance of pus, cancer cells, etc., may bring about thrombosis.

(*c*) The metabolic product of certain micro-organisms seem to be powerful fibrin ferments; among these may be mentioned especially those of pneumonia and diphtheria.

(*d*) Extensive burns, possibly by the loss of fluid from the blood, are occasionally followed by thrombosis.

2. **Changes in the Vessels.**—Diseases leading to thickening, and roughening of the intima with deposition of calcareous salts are particularly to be mentioned, and of these arteriosclerosis is the most important. Endocarditis with calcification produces coagulation of the blood less often than might be imagined. In *aneurysms* the irregular and uneven vessel walls almost invariably predispose to thrombosis. Inflammatory changes in or near the vessel walls, with resulting changes in the intima, are not infrequently followed by thrombosis.

Ligation of the vessels, which causes laceration of the delicate internal coat, is constantly followed by thrombosis. The presence of one thrombus in a vessel always tends to the formation of others, extending higher and involving new portions of the vessel. Thus, using a rather common example, if a thrombus form in a small branch of the internal iliac vein, it may gradually extend to the internal iliac vein and project into it. A new thrombus may be then formed within the larger vein, extending to the junction with the external iliac vein, which in its turn may become blocked, and a continued growth of the thrombus, extending along these vessels, may continue down the leg, producing the not uncommon disease known as *phlegmasia alba dolens* or "milk leg."

3. **Changes in the Speed of the Circulation.**—These are rather fruitful sources of thrombosis. The thrombi found post mortem within the heart and great vessels are probably formed during the death agony or just after death. As the blood current slows the white corpuscles show a disposition to adhere to the walls of the vessels. Blood plaques are deposited upon them so soon as the leukocytes cease to move, and the resulting mass, which appears hyaline from degeneration of the plaques, extends into the lumen of the vessel. Fibrin is almost immediately deposited upon this, corpuscles become entangled in it, and soon a more or less solid mass or thrombus is formed. The thrombus may be yellowish, grayish, or red according to the number of red corpuscles it contains. When the current is slowed the nutrition of the part supplied by the vessels is altered and the chemistry of the blood becomes changed, this variation from the normal itself tending toward thrombosis.

Structure and Variety of Thrombi.—Thrombi are usually composed of superimposed layers of fibrin, entangling a variable number of red and white corpuscles. They are commonly distinctly laminated or stratified upon naked-eye examination, the lamina sometimes varying considerably in color and thickness. The longer the thrombus remains within the body the firmer and dryer it becomes and the more closely it adheres to the vessel walls. The coagula formed in the heart and great vessels after death are dark-red masses of soft, jelly-like consistence, not adherent, and aptly described as like "*currant jelly.*" They are either uniform in structure or the fibrin and corpuscles are found to occupy different levels, so that the upper part of the clot is of a pale yellowish color, containing only fibrin and leukocytes, and said to resemble "*chicken fat,*" while the lower part resembles currant jelly. Such mixed clots are formed slowly after death. When the coagulation has been ante mortem, the fibrinous mass is quite adherent to the columnæ carnæ, and is fibrillar, sometimes tough and firm, sometimes friable. The older the thrombus the paler and more brittle it becomes. Fresh thrombi are firm and elastic. Certain hyaline thrombi are thought to depend upon agglutinated erythrocytes without the formation of fibrin.

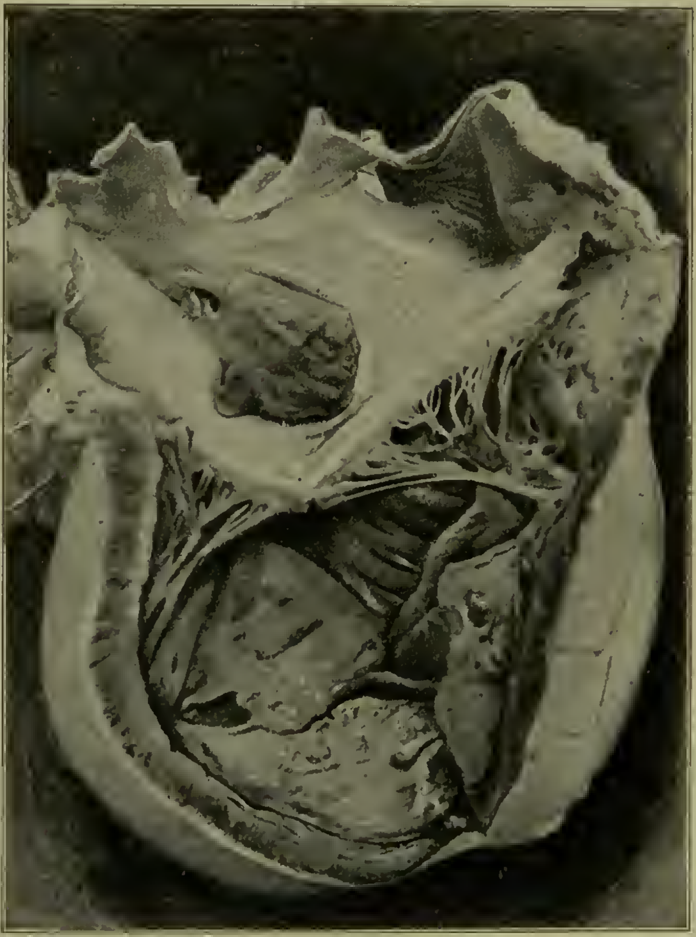

FIG. 34.—Heart with intraventricular and intra-auricular thrombi. From a specimen in the museum of the Philadelphia Hospital.

Classification of Thrombi.—1. **According to their Etiology.**—(*a*) *Infectious thrombi.* These depend upon bacteria which have gained entrance into the circulation through wounds, ulcers, etc. Such thrombi are apt to occur in the intestinal vein in dysentery, and by extending and distributing themselves may bring about metastatic abscesses and pyemia.

(*b*) *Mechanical thrombi.* These forms have already been described.

2. **According to the Period of their Formation.**—(*a*) *Primary* or *initial thrombi,* and

(*b*) *Secondary* or *consequential thrombi,* which depend upon a preexisting thrombus.

3. **According to their Morphology.**—(*a*) *Central*, *occluding*, or *obstructing thrombi*, which are formed by the conversion into a thrombus of the entire blood mass contained within a certain portion of a vessel. Such thrombi follow the application of a ligature to a vessel, and usually extend from the seat of ligation to the first collateral branch.

(*b*) *Parietal thrombi* which are attached to the wall of the vessel, and consist of successive layers of fibrin and corpuscles. They do not obstruct the vessel, or do so only partly, the circulation continuing around or through them. They are most commonly seen in aneurysms; their structure is distinctly laminated.

(*c*) *Valvular thrombi* are parietal thrombi that take the form of one of the valves seen in the veins. They are in reality simply parietal thrombi that have become partially detached from the vessel wall.

(*d*) *Channelled* or *tunnelled thrombi* are of annular form, leaving but a small channel in the center, through which the circulation continues. The circulation of the blood through a thrombus in this way is not always due to the original form of a thrombus, but may be the result of subsequent cavernous changes in old thrombi.

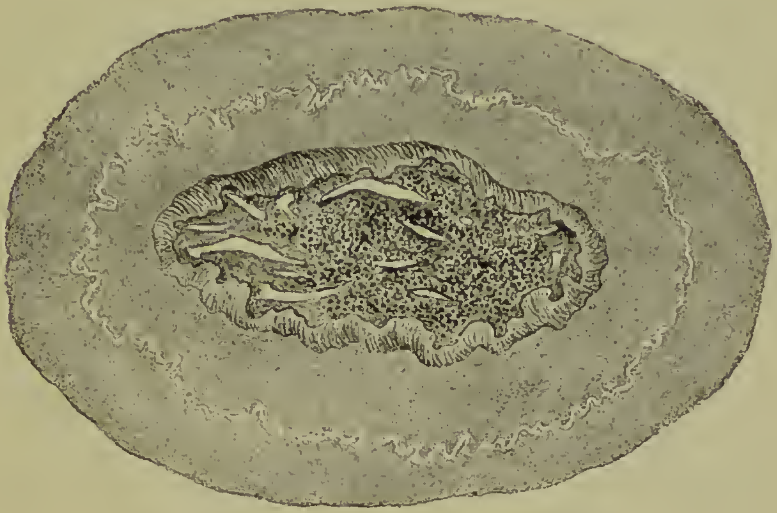

FIG. 35.—Central or occluding thrombus (Orth).

(*e*) *Ball thrombi* are rounded thrombi that occur in the chambers of the heart, chiefly in the auricular appendages. They vary in size from a pea to a hen's egg, and may be quite loosely attached to the auricular wall.

(*f*) *Polypoid thrombi* are ball thrombi with pedicles.

Metamorphoses of Thrombi.—1. *Organization.*—By the organization of a thrombus is meant its replacement by fibroconnective tissue. It is not the transformation of the thrombus into connective tissue. The exact nature of the process will be better understood after the phenomena of inflammation and cicatrization have been described. The new connective tissue that takes the place of the thrombus is an outgrowth of the intima of the blood vessel, whose endothelial cells multiply, impinge upon and penetrate the clot, and gradually develop into fibrillar tissue. As this is taking place the original substance of the thrombus slowly disappears, partly by absorption and partly through the agency of leukocytes, which by their phagocytic action remove particle by particle the detritus of broken down corpuscles, and partially softened fibrin. The new connective tissue is gradually vascularized as its formation is perfected by newly formed capillary vessels that extend into it from the vasa vasorum. Ultimately the coagulum entirely disappears and a solid connective tissue cylinder replaces the original vessel. The occlusion is not permanent in all cases, but after a time becomes channelled, so that the circulation may be re-established, at first through the very small channels, later through larger ones, in what seemed destined to remain a solid tissue. These reactive changes are commonly spoken of as *thrombo-arteritis* or *thrombophlebitis*.

2. *Liquefaction or Softening of Thrombi.*—This is a retrogressive change. While the endothelial cells of the intima are beginning to encroach upon and penetrate the coagulum, its interior undergoes rapid destruction, so that the central part softens and becomes semi-fluid or even fluid. The blood pigment that may have been present is liberated, and imparts a reddish color to the softened mass. When examined microscopically the softened material is found to consist of granular matter with a few leukocytes. Occasionally the leukocytes are so numerous that the softened mass has a creamy appearance. It was formerly thought that thrombi of this kind had suppurated. Of course, there may be infected thrombi, but thrombi presenting this creamy appearance are found by bacteriologic examination to be sterile, and the microscope shows the creamy substance to be molecular detritus without pus corpuscles. Softening is particularly marked in thrombi of the heart, possibly from the natural maceration favored by the surrounding blood. It is said that the softening of the thrombus is favored by febrile conditions. In the process of softening rupture may occur and the softened contents of the mass escape into the blood. At other times fragments of the thrombus itself become detached and enter the circulation. As these circulating particles in their passage reach vessels of smaller and smaller caliber, there is always danger that at some point of bifurcation the vessel will become too small to admit them and that they will lodge and obstruct the circulation. Such a plug is known as an *embolus*.

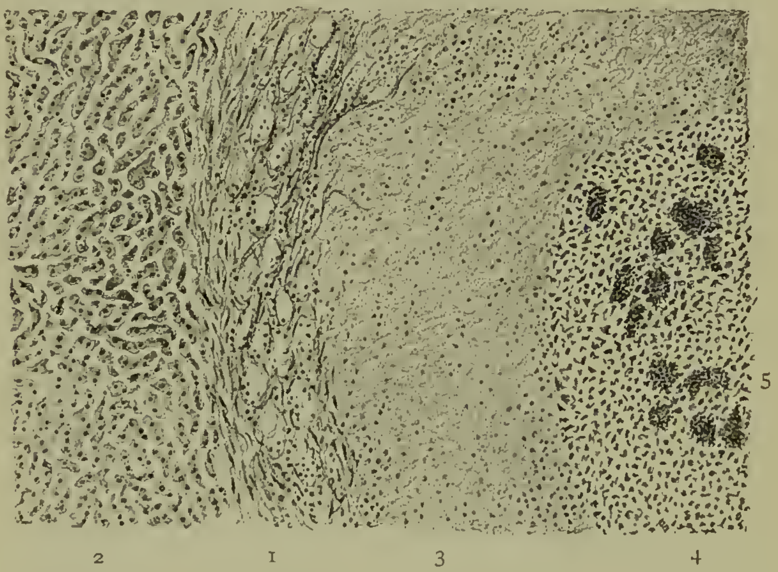

FIG. 36.—Pylethrombophlebitis mycotica—mycotic, purulent, embolic thrombosis, and inflammation of the wall of the portal vein: 1, Wall of the branch of the portal vein with inflammatory infiltration; 2, liver tissue; 3, zone of necrosis; 4, pus; 5, groups of bacteria.

3. *Calcification* of thrombi is common, especially in small venous thrombi, and leads to the formation of *phleboliths* and *arterioliths* (*q. v.*).

EMBOLISM.

Embolism is intravascular obstruction from the lodgement of a solid body. Any circulating body is an *embolus.*

Etiology.—Among the more frequent emboli are scraps of thrombi, detached vegetations from diseased valves of the heart, clusters of microorganisms, groups of cancer cells, globules of oil, and air.

Seats of Occurrence.—The process may occur in the systemic pulmonary or portal circulation, either in the larger vessels or in the capillaries. As a rule, embolism occurs in the smaller arteries, some of which, from their position, seem particularly predisposed to it. Thus, it is more common in the left carotid artery than the right, the left iliac than the right, and the right pulmonary than the left. The superior and inferior mesenteric arteries are practically exempt. In the brain, where they are rather common, emboli usually follow the middle cerebral artery, and are particularly prone to lodge in the artery of the corpus striatum.

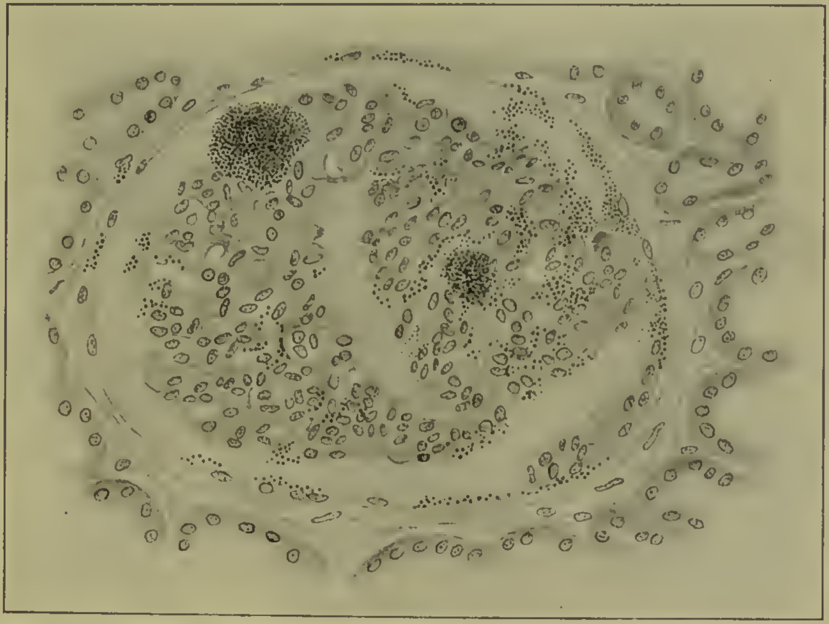

FIG. 37.—Infectious embolism of the kidney following endocarditis and showing groups of staphylococci in a glomerulus (Dürck).

Varieties of Emboli.—Emboli are described as *mechanical* or *simple emboli*, and *specific* or *infectious emboli.* Of the two, the infectious emboli are the more damaging, containing as they do bacteria, whose entrance into the tissues commonly causes suppuration.

Results of Embolism.—1. **Thrombosis.**—Embolism is invariably followed by thrombosis, probably both in the proximal and distal portions of the vessel, as far as the collateral circulation. The cause of this thrombosis is evident: the circulation is stopped, the wall of the vessel impinged upon by a foreign body, and the stagnated blood changed in composition. The embolus may be inconspicuous in size in comparison with the secondary thrombosis that it causes, and be so surrounded by the thrombus as to be found with difficulty.

2. **Inflammation of the Vessel.**—Inasmuch as the embolus is an injurious foreign body, inflammation of the vessel walls is apt to be the outcome of its lodgement.

3. **Interruption of the Circulation.**—The interruption of the circulation will vary in effect according to the size of the vessel obstructed, the degree of obstruction as controlled by collateral circulation, and the facility with which the collateral circulation can be set up.

(*a*) *Gangrene.*—If the principal artery of the limb be obstructed in such a way that adequate collateral circulation of the limb itself or of the fingers or toes cannot be set up, gangrene will result.

(*b*) *Necrosis.* — Necrosis occurs chiefly in the internal organs when portions of them are robbed of nourishment that cannot be derived from other sources.

(*c*) *Atrophy.* — It occasionally happens that when an artery is obstructed anastomoses form sufficient to maintain the vitality of the part, but insufficient to maintain its normal integrity. Atrophy consequently results.

(*d*) *Aneurysmal Dilatations.* — These are rare as the result of embolism, and are usually to be seen in the cerebral arteries.

(*e*) *Infarction.*—In its broad sense infarction means obstruction. In the sense here employed it refers to the circulatory disturbances caused by the obstruction—that is, the formation of infarcts. An *infarct* is a tissue area whose nutrition is prevented by embolic obstruction of its vessel. Infarcts may be described as *anemic* and *hemorrhagic*. An *anemic infarct* or *white infarct* is a bloodless tissue area resulting from embolic obstruction. A *hemorrhagic infarct* is a blood-saturation area of embolic obstruction. Infarction takes place only in organs in which there are end-arteries—that is, arteries terminating in veins, without anastomoses with other arteries. Anemic infarction results in the formation of a pale grayish or yellowish conical-shaped area of necrotic tissue. It is simple in formation and easily understood.

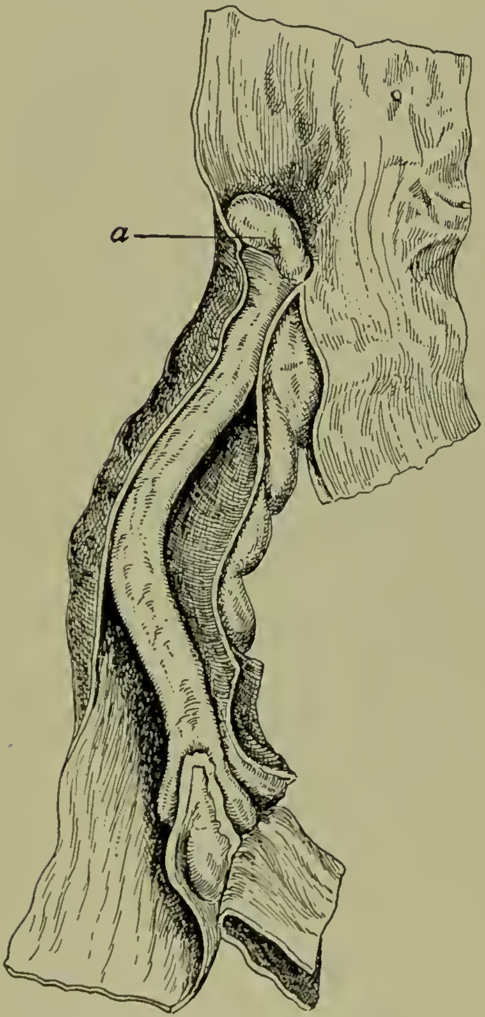

FIG. 38.—Thrombosis of the aorta. At *a* a large embolus is lodged at the beginning of the right common iliac artery, which is occluded by a secondary thrombus, causing gangrene of the corresponding extremity and necessitating amputation. The embolus was a clot from a heart-valve the seat of extensive inflammation (Hektoen).

Hemorrhagic infarction is rather complicated. The immediate result of the arterial plugging may be anemia in its distribution; but later the tissue becomes engorged with blood from one or the other of several sources. Cohnheim was of the opinion that the blood regurgitated into the infarcted area from the veins. Others think that the end-arteries have anastomoses with minute vessels near their termination—for example, the interlobular arteries of the kidneys may possibly have anastomoses with small vessels descending into the substance of the organ from its capsule—and hold that the capillary engorgement depends upon the entrance of blood from these sources. Still others hold that the blood does not escape from the obstructed vessels through the capillaries, but is held in place by the embolus until anemia or degeneration of the walls of the vessel allow it to escape into the tissue. Lastly, it is thought that the formation of the hemorrhagic infarction depends upon reflex contraction of the vessels on the proximal side of the embolus, so that an excess of blood is forced into the adjacent capillaries, which rupture.

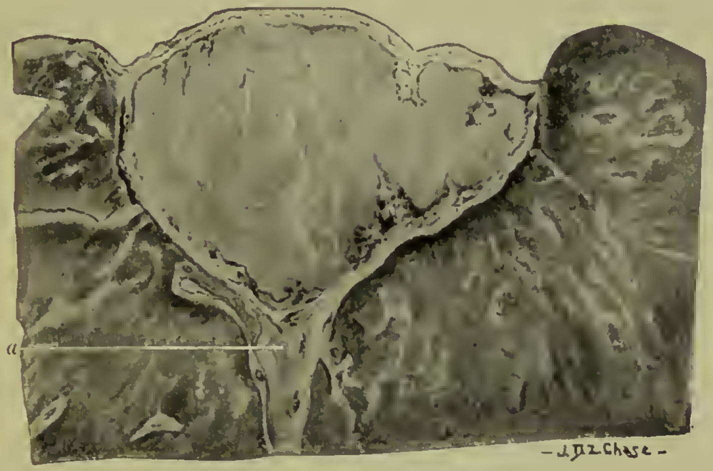

FIG 39.—Hemorrhagic infarct of the spleen. The infarct, which is old and in the stage of cicatricial induration, is pale and homogeneous. It is distinctly encapsulated by newly formed connective tissue, within which is a dark line of hemosiderin pigmentation. The vessel with the organized thrombus is well shown at *a*. Magnification, four times normal.

The engorgement in the infarcted area is an interstitial hemorrhage, resulting from the escape of the blood through the injured or diseased vessel walls. In its early stages the infarct is dark red, its substance friable or mushy. Retrogressive changes soon set in. The neighboring healthy tissue then resents the contact of the infarcted area and a zone of inflammatory hyperemia develops about it. As the degenerative changes take place within the infarction itself, a productive proliferation of connective tissue takes place on the outside, so that in a short time the diseased area is walled off from the healthy tissue by a connective-tissue rind. As time passes on the dark-red color of the infarcted tissue becomes paler by the removal of the

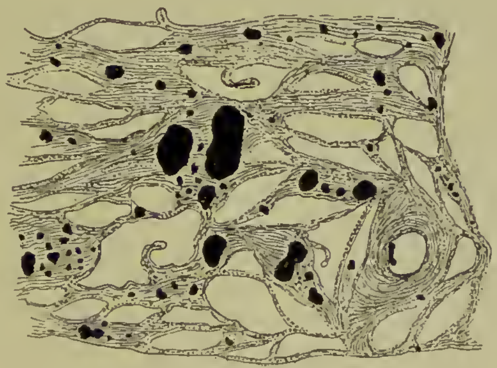

FIG. 40.—Fat embolism of the lung after fracture of the femur. The fat globules and masses, stained black with osmic acid, lie in the capillaries of the lung. × 150 (Hektoen).

blood pigment, and a grayish solid mass remains. It is structureless to the naked eye, and on microscopic examination seems to be made up of a molecular débris consisting of destroyed blood corpuscles, fibrin masses, occasional fibers and remnants of cells of the tissue in which the infarction took place. Degeneration progresses, and in the course of time the absorption of the detritus leaves nothing but the fibroconnective-tissue envelope, firmly contracted into a cicatrix, which draws upon the surface of the organ so as to produce a distinct pucker, at the bottom of which a somewhat stellate scar is visible. Sometimes calcareous deposits take place in the necrotic tissue, forming stony masses in the organ or upon its surface. Should the embolus be *infectious*, abscess formation instead of infarction may occur.

Fat Emboli.—These usually occur after fracture of the shaft of the long bone, with rupture or laceration of the blood vessels, by which fat globules enter the circulation. The fatty globules are unable to find their way with equal facility through the small vessels, and in consequence plug them. Fatty emboli usually lodge in the lung.

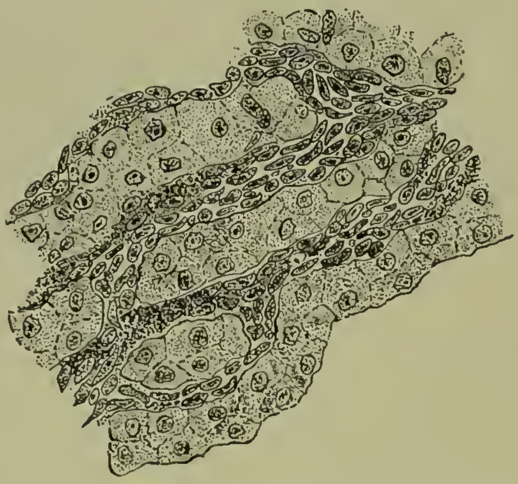

FIG. 41.—Embolism of pigmented sarcoma cells into capillaries of the liver. The intrahepatic capillaries are filled to distention with spindle-shaped cells containing brown granular pigment. The liver was uniformly brownish black, and enlarged to many times its normal size on account of this diffuse infiltration with tumor cells. The primary tumor was a melanosarcoma of the eye. Müller's fluid, celloidin, hematoxylin, and eosin. × 2500 (Hektoen.)

Air Emboli.—The entrance of air into the circulation is usually regarded as extremely dangerous. The air globules seem to be absorbed with slowness, and are capable of obstructing the capillaries in which they lodge. The entrance of globules of air into the right ventricle of the heart seems to embarrass the movements of that viscus, which is not always able to discharge the air with the blood. The collection of any quantity of air in the heart is fatal. The injection of 1 c.c. of air into the ear vein of a rabbit is sometimes followed by instant death. The injection of air beneath the skin is without danger.

Pigment emboli are occasionally seen in the melanemia of intermittent fever. The blood contains numerous granules of pigment, formed by the parasite from the blood corpuscle upon which it preys. With the sporulation of the parasite the pigment granules are set free, and, clustering together, form sufficiently large masses to collect in the capillary vessels.

Anthracotic embolism occurs in advanced cases of anthracosis, where the accumulation of coal particles in the bronchial lymphatic glands finds its way by ulceration into the venous system, thus being distributed. The blackish deposits resulting from the distribution of the coal dust are found in the liver, kidneys, spleen, brain, etc.

Micro-organismal emboli are frequently observed in the infectious diseases, and are formed by the entrance of bacteria into the circulation, usually through the venous system. They are of interest only when they bring about suppuration or necrosis.

Parasitic Emboli are very unusual. There is, however, a certain worm, the *Strongylus armatus*, which, entering the circulation of the horse, finds its way to the mesenteric artery, and by lodging in it sometimes causes the formation of a small aneurism. This worm does not occur in man.

CHAPTER V.

CHARACTERISTICS OF CELL LIFE.

THE CELL.

THE cell is the element of vital organization. Living beings may consist of one or many cells (*protozoa, metazoa*). Every perfect being with its elaborated tissues and organs is the consummation of cellular energy; and every organ and tissue, whether in health or disease, consists of cells or their derivatives. Indeed, no matter how complex its parts or multitudinous its elements, the entire organism springs from a single cell, the ovum. The life of an organism is but the sum of the activities manifested by its cells. When the cellular manifestations progress so as to maintain a regular equilibrium, the resulting condition is described as *health*. Should any of the activities preponderate over others, or some cease while others continue, a variation from the normal condition must occur, this variation constituting what we call *disease*. When the cellular activities entirely cease, *death* is inevitable. No wonder that Virchow called the cell the "unit of life!"

To the pathologist, therefore, the entire organism consists of an enormous highly specialized cellular community, whose individuals are all of interest because of the peculiar interdependence in which they exist, and the constructive and destructive activities which they manifest. Nothing can be hoped from any study of diseased conditions that does not first consider the cellular changes.

As has already been pointed out, the perfected animal body develops from a single cell, and in its developmental stages every tissue is cellular. It is, however, an error to look upon one of the higher animals as consisting of an aggregation of cells, or as someone has facetiously expressed it, "a mountain of amebæ." The completely formed organism has in large part ceased to be cellular and is formed of tissues, of which some, like the crystalline lens, are entirely without cells, others, like bone, tendon, and cartilage, relatively poor in cells, and a few, such as the liver and spleen, principally made up of cells.

The non-cellular portions of the tissue are described as intercellular substance, and are all cell derivatives, not metabolic, and exhibiting no phenomena of life. Taken by themselves, the lamella of the bones, the fibers of yellow elastic and areolar tissue, and the *liquor sanguinis* are practically without life, but the integrity of them all depends upon the life and health of the cells of the tissue to which they belong.

Simple as the structure of the cell may appear at the first glance, it is in reality very complex. Ordinarily a cell is a small nucleated protoplasmic mass. Enclosing certain cells we find a thin, delicate membrane or capsule, sometimes consisting of an actual rind, sometimes being nothing more than a condensation of the outer layers of the cytoplasm. This envelope is described as the *cell wall*, or if about an ovum as the *zona pellucida*. When not forming a distinct envelope, but constituting an induration of the protoplasm, it is better described as an *ectosarc*. Comparatively few cells possess distinct walls. All of the substance circumscribed by the cell wall is known as *cell contents*, the greater part being a granular, jelly-like substance, the *protoplasm* or *cytoplasm*.

Careful examination shows the cytoplasm to be divided into a granular part, or *spongioplasm*, forming the central mass, and a homogeneous substance called *hyaloplasm*, best seen where it forms the ectosarc. The granules of the spongioplasm are called *microsomes*.

The true structure of cytoplasm is not comprehended by the terms spongioplasm and hyaloplasm. Frohman thought he made out the existence of a spongy framework, and suggested that the spongioplasm formed a reticulum which floated in the hyaloplasm. Bütschli believed the true structure to be a chambered or honeycomb arrangement. Flemming thought he found a distinct filamentous arrangement of mitome and paramitome.

The usually accepted view of cytoplasmic structure is that it is a granular jelly. Altman, who holds this view, goes to a possible extreme in looking upon the granules as the essential vital elements, to which he gives the name *bioblasts*. The bioblasts are identical with the microsomes above mentioned.

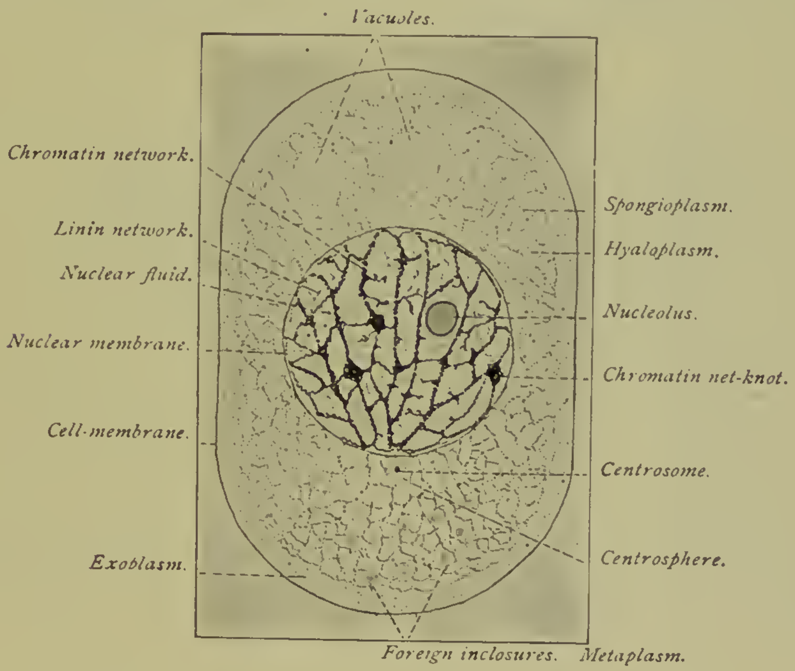

FIG. 42.—Diagram of a cell.

To the eye cytoplasm appears as a semi-fluid, adhesive, colorless, strongly refracting, jelly-like mass. It does not mix with water, is alkaline in reaction, and is probably composed chemically of $C_{72}H_{106}N_{18}SO_{22}$. The characteristic of cytoplasm is the presence of a large amount of *plastin*.

Among the cytoplasmic granules some have an affinity for eosin, the *eosinophilic granules*; others have an affinity for methylen-blue, gentian-violet, etc., the *basophilic granules*; and still others an affinity for hematoxylin, the *neutrophilic granules*. Within the cytoplasm it is not uncommon to find granules of matter not belonging to the cell, but temporarily contained within it; these are called *deuteroplasm*. Among the granules of the deuteroplasm, those of fat and glycogen are common in the cells of the liver. Some of the deuteroplasmic granules seem to consist of substances absorbed by the cytoplasm, others of substances elaborated by it.

Every cell is provided with a "circulating albumin" apart from its cytoplasm, but circulating within it and carrying nutriment to all its parts.

Every vital functional cell contains a *nucleus*. This is a small cell-like body within the cell. It consists of a structureless surrounding *nuclear membrane*, *nuclear substance*, and *nuclear juice*. The nucleus is usually spherical or ovoid in shape, and is not variable, the nuclei of healthy cells of the same kind being almost exactly alike. The nuclei of a few cells, as the polymorphonuclear leukocytes, on the other hand, are characterized by extreme irregularity, sometimes appearing club-shaped, sometimes horseshoe-shaped, and sometimes distinctly lobulated. There are also peculiar branched nuclei in some of the cells of the lower animals. The nucleus usually occupies a slightly eccentric position in the cell, but may at times be at the center. It seems to be movable, and in pathologic conditions seems to occupy the part of the cell whose nutrition is best—*i. e.*, the peripheral part, as in the giant cells of tubercle.

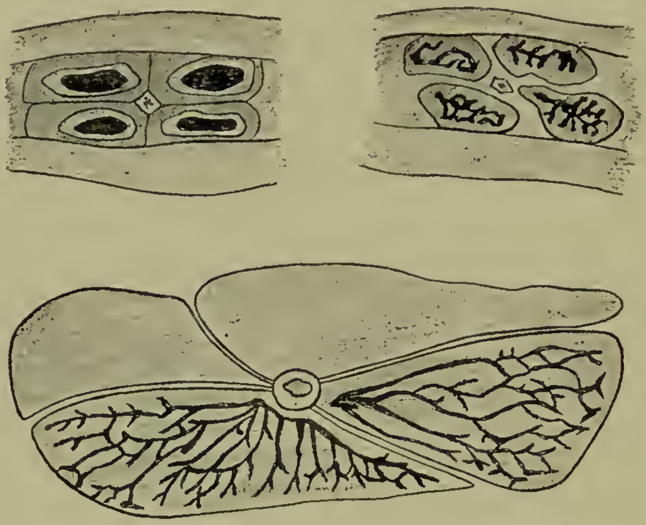

FIG. 43.—Nuclei of various shapes, some vesicular, some branched, some dendritic (Mayer).

The nuclear substance or *karyomitome* consists of a fibrillar material, forming a coarse network, which generally can be seen in stained specimens. Karyomitome is probably complex in structure or variable in composition, as certain parts of it having an affinity for the nuclear stains are described as *nuclein* or *chromatin*. This is a substance with a pronounced affinity for alkaline dyes, such as borax and lithium-carmin and hematoxylin solutions. It swells in water and in feebly alkaline solutions, and is dissolved in strong solutions of NaCl, $MgSO_4 + 7H_2O$, K_2HPO_4, also in HCl, $KFeCy_6$, and $C_2H_4O_2$;

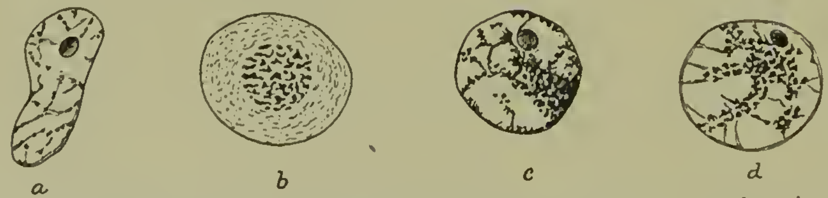

FIG. 44.—Changes in the nucleus caused by activities preliminary to karyokinesis: *a*, Resting nucleus of spermatoblast of Asiaris megalocephalus; *b*, similar nucleus from the growing or active cell; *c*, resting cell from developmental zone; *d*, some cell preparing for division.

it is digested by trypsin. Nuclein always contains considerable (about 3 per cent.) phosphoric acid, usually combined with some of the albumins so as to form nucleinic acid. Some chromatin is present in every nucleus, but the quantity varies, being relatively greater in the nuclei of lymphoid than in those of epithelial tissues. The arrangement of the chromatin in the nucleus varies: sometimes it appears granular, sometimes reticulated, sometimes filamentous. By *linin* or achromatin is meant the nuclear filamentous substance that cannot be stained.

The nuclear juice is called *karyoplasm;* it is a homogeneous jelly, about which nothing is known. It is frequently precipitated by fixing-reagents, the granules thus formed being known as *paralinin.*

The *nucleolus* is a more or less distinct, in some cases (the ovum) circumscribed, body within the nucleus, which consists principally of a substance known as *paranuclein* or *pyrenin,* some of which exists in every nucleus.

Exactly what the nucleolus is has not yet been determined. No doubt the germinal spot of the ovum and the nucleoli of nerve cells are distinct, definite bodies, but, in the majority of cells, what are called nucleoli are in part nuclein or chromatin bodies and in part linin bodies. At times the appearance called nucleolus may be nothing more than the point at which chromatin fibers cross one another.

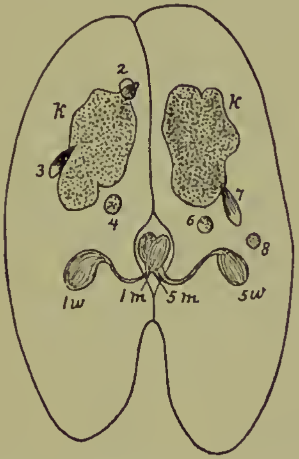

FIG. 45.—Conjugation of paramœcium showing the interchange of nuclear substance (R. Hertwig).

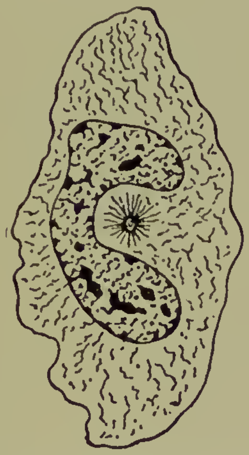

FIG. 46.—Leukocyte of a salamander larva showing the centrosome surrounded by a radiating attraction sphere (Flemming).

Paranuclein colors best with acid stains, and has none of the chemical peculiarities described for nuclein.

The nuclear membrane, whose existence Hertwig has demonstrated, consists of a substance known as *amphipyrenin.*

As a rule, each cell contains a single nucleus, though a few cells, like those of the liver, frequently contain two. Pathologic cells, like the giant cells of tubercle or sarcoma, may contain hundreds of nuclei. The size of the nucleus is usually proportionate to that of the cell, though in epithelial cells the nuclei are proportionally much smaller than in lymphoid cells. The eggs of some of the snakes and amphibians have very large nuclei.

Cornil and others have described a small body, or *paranucleus,* as present in certain cells. It forms a somewhat indistinct mass, rarely definitely outlined, generally occupying the cytoplasm opposite the position of the nucleus. The significance of this body is somewhat uncertain. By some it is looked upon as a kind of nuclear excrement. Among the infusoria it appears to be an important organ in cellular conjugation and reproduction.

Many cells, especially the ovules of different animals, contain small spherical bodies known as *centrosomes*, which play an important rôle in cellular division, but which are not yet fully understood. The centrosome sometimes occupies a central position, sometimes a polar position, in the cell. Sometimes the centrosome is surrounded by a finely granular area called an *attraction sphere*.

To be a true cell in the anatomic sense, two parts, the *cytoplasm* and the *nucleus*, must be present. Cells, such as the red blood corpuscles, without nuclei are to be looked upon as cell derivatives no longer able to manifest the essential properties of life.

The size of the cell is subject to great variation, the causes which govern the size not being known. It has been suggested that the cause is physical, it being a well-known fact that as spheres increase in size the increase of the contents is vastly out of proportion to the increase of surface, so that there must come a time when it would be impossible for the surface to absorb sufficient nourishment to support the interior. While this is no doubt true as an explanation why cells must always remain small, it does not explain why some should be smaller than others. Thus, the leukocytes are quite small cells, while the ovum and the corpuscles of Purkinje in the cerebellum are enormous cells visible to the naked eye, and the cells of the striated muscles are sometimes an inch long. Motility may have something to do with it, as may also the amount of work performed by the cell. Those which move rapidly, like the leukocytes, are small; those which functionate actively are also small.

The shape of a cell depends partly upon its environment, partly upon its specialization. The ovum and the great majority of embryonal cells are spherical, hence this shape is supposed to indicate the primitive condition. As resting amebæ are commonly spherical, sphericity is supposed to indicate inactivity of the cell. Certain cells are obliged to accommodate themselves to the interstices of the tissue, and become elongate, stellate, fusiform, or cuboidal accordingly. When many cells are so crowded together as to press upon one another they may be polyhedral, a section passing through them giving each the appearance of a minute hexagon. The shape of the cell is also considerably influenced by its function. Cells designed to cover surfaces are often flat and squamous or scale-like. Upon surfaces exposed to friction the cells are arranged in many layers, cells upon delicate protected surfaces free from all possible injurious contacts in a single layer, sometimes flat, sometimes cuboidal, sometimes columnar.

In the higher animals cellular movement is restricted, the performance of specialized functions requiring that the cells of the organs shall be fixed and not free to wander, so that the higher their specialization becomes the less independent become the cells and the more restricted their movements. It is not always specialization that restricts movement, however, as the cells enclosed in the lacunæ of cartilage and bone have their movements restricted by the nature of their environment, although of lowly specialization. The cells of the blood are the most free and independent of the body's cells, those of the connective tissues taking second place. The secretory cells of the epithelial glands, the covering epithelial cells, and the nerve cells are probably devoid of individual movement. Between the extremes mentioned there is a series of cells whose individuality, motility, and independence become less and less as their specialization becomes more and more important.

There are two forms of cellular motility, the *ameboid movement* and the *ciliary movement.*

Ameboid movement is motile power similar to that of the ameba. It consists in a flowing of the protoplasmic jelly, by which numerous rounded prolongations known as *pseudopodia* form on the surface of the cell. Ameboid cells usually present a number of pseudopods of various lengths extending in different directions. They consist primarily of hyaloplasm, but no sooner attain a length equal to their breadth than the granules of the spongioplasm may be seen flowing into them. The inflowing of the granular cytoplasm causes an increase in the size and length of the pseudopod, with a concomitant diminution in the size of other pseudopods. If the cytoplasm continue to flow in one direction the pseudopod grows larger and larger, extends smaller pseudopods, and the withdrawal of the cytoplasm from its original position into the pseudopod is accompanied by some movement of the entire cell. By thus extending pseudopodia into which the cytoplasm flows from positions originally occupied, the cell slowly moves here or there as attracted by food particles or other forces.

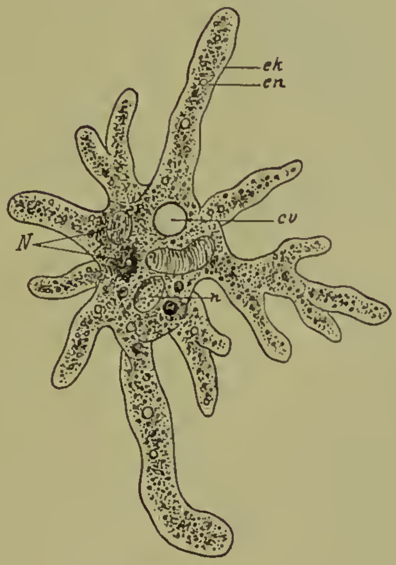

FIG. 47.—Amœba proteus: *n*, Nucleus; *cv*, contractile vacuole; *N*, nutrient material in process of digestion; *p*, pseudopod; *en*, endosarc; *ek*, ectosarc (from R. Hertwig).

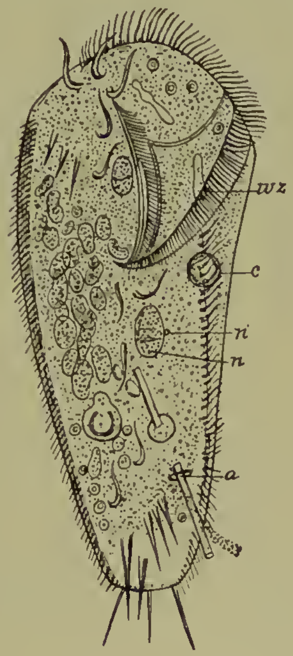

FIG. 48.—Stylonychia mytilus: *wz*. Cilia about the mouth opening; *c*, contractile vacuole; *n*. nucleus; *n'*, nucleus; *a*, anus (Clau's *Zoology*).

The pseudopods of the ameba are large in proportion to the body of the cell, and form blunt, rounded, club-like projections. Those of the radiolaria are elongate, slender, and branched. The pseudopods of the leukocytes and of other body cells of the higher animals are usually short and blunt.

Intracellular circulation of the cytoplasm is is a phenomenon witnessed among vegetable cells and among a few of the lowest unicellular forms of animal life. It is not observed within the cells of the higher animals, although it probably exists. The circulatory movement consists of a very slow rotary movement of the cell fluids, which carry some or all of the granules with them. The phenomenon probably has something to do with the nutrition of the cell.

Ciliary movement is accomplished by certain processes of the cells known as cilia or flagella. Cilia are short, rigid, bristle-like projections; flagella longer, waving, hair-like processes. Two forms of ciliary movement are observed: in one the cells are driven onward by the lashing cilia; in the other, the cells being fixed, the lashing of the cilia carries onward whatever fluids or minute solids come in contact with them. Cilia are very abundant among the unicellular animals, performing all sorts of functions for them. Thus, in the paramecium or slipper animalcule there are two sets of cilia of different lengths, one consisting of short, bristle-like projections, which seem to cover the entire body and serve the purpose of locomotion; the other, situated about the mouth-opening, are longer and direct the food into it.

The cilia are specialized protoplasmic prolongations which project through minute openings in the cell wall. They are permanent, and not, like the pseudopods, susceptible of projection and retraction at will.

Of the cells of the higher animals, the spermatozoa are almost universally provided with a flagellum, by means of whose lashings the cell is driven onward to the ovum. In the molluscs cilia are of vast importance in properly circulating the fluids through their siphons, while in the higher animals they are found upon the epithelial cells of the pharynx, trachea, Fallopian tube, vas deferens, etc. In the human body there is but one cell propelled by a flagellum, the spermatozoön. All the other ciliated cells are fixed, the cilia directing currents of fluid, etc. These cells usually possess a number of cilia projecting from the free extremity. The movement of the cilia is regular, undulatory, and always in the same direction, the cilia of neighboring cells moving in unison, and the vibrations occurring many times a second. Ciliated infusoria seem to possess the power of regulating the movements of the cilia at will, and in cases of cellular conjugation the cilia of the conjoined individuals move synchronously.

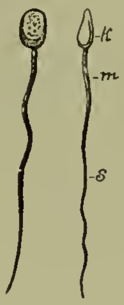

FIG. 49.—Human spermatozoa seen from two different aspects and showing the peculiar flattened and excavated head: *k*, Head; *m*, body; *s*, tail or flagellum (Hertwig).

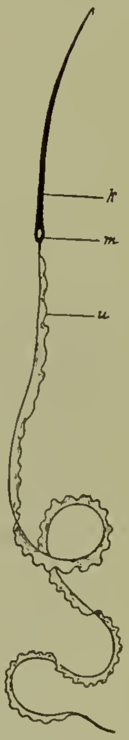

FIG. 50.—Spermatozoön of Salamandra maculata: *k*, Head; *m*, body; *u*, undulating membrane attached to flagellum or tail (Hertwig).

Nutrition of the Cells.—According to their specialization we find the cells losing more and more the manifestations of independent existence. Thus, certain of the cells perform a phenomenon, common among free unicellular animals, called *phagocytosis*, and exert themselves as scavengers of the tissues for the removal of bacteria and inert and effete particles.

Phagocytosis, a phenomenon of ameboid cells, is the incorporation of particles of solid matter by the cells. It is commonly observed in the ameba, which, for purposes of nutrition, constantly takes into its cytoplasm minute plants, such as bacteria, diatomes, desmids, algæ, etc., and by its enzymes dissolves or digests the useful parts, the effete matter being extruded. In the performance of this act the ameba exerts a definite selective tendency, usually refusing to take up useless particles. Adapted nutrient materials seem to exert an attractive force upon the little animal, which apparently moves about in search of them. The attractive force has been called by Pfeffer *chemotaxis*, *chemiotaxis*, or *chemotropism*.

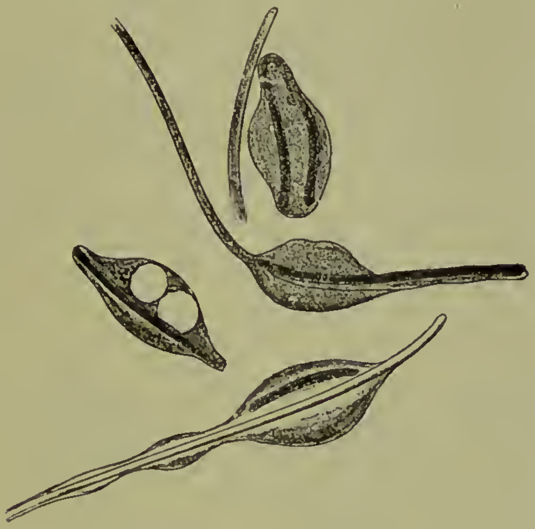

FIG. 51.—Phagocytic cells with incorporated bacilli (Metschnikoff).

The cells of the higher animals manifest the same phenomena to a certain degree, the more independent cells having greater capabilities in this direction than those fixed and specialized. No cell possessed of a rigid cell wall would be able to take up extraneous bodies, so that it is a phenomenon shown by few, and essentially by the ameboid cells.

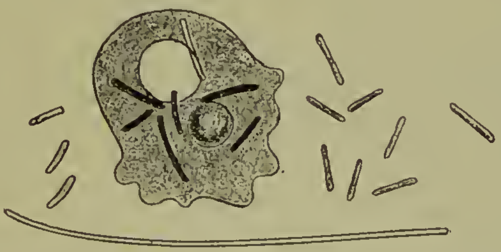

FIG. 52.—Leukocyte with incorporated bacilli illustrating phagocytosis (Metschnikoff).

The leukocytes form the chief phagocytic cells of the body, and so become its chief scavengers. Of the leukocytes, the eosinophilic and polymorphonuclear forms are most markedly ameboid. Phagocytosis is, however, almost universal among the connective-tissue cells, and is occasionally observed in epithelial cells. Nervous and muscular cells probably never manifest the phenomenon.

The cells of the body are far less sensitive and selective than the ameba, for though the ameba moves about in search of food and responds essentially to nutritive impulses, the body cells move in response to stimuli caused by all sorts of inert particles. It is an interesting fact that different substances operate differently upon the leukocytes, some attracting them (positive chemotaxis), others failing so to do (negative chemotaxis). Bodies that are positive in their chemotactic influence are by no means all useful to the leukocytes, nor are all the negatively chemotactic substances inert or injurious to them. The phenomenon seems to depend solely upon chemical or electric affinity.

Associated with phagocytosis and, according to the theory of Metschnikoff, of vast importance to health is the phenomenon of intracellular digestion. Sometimes the particles taken up by leukocytes and other phagocytes are simply dropped again, sometimes they are passed on to other cells, sometimes they are dissolved or digested by the cells through enzymes which he calls *macrocytase* and *microcytase*. This intracellular digestion is of the greatest importance when the incorporated bodies are bacteria or other parasites capable of doing mischief in the body. If they are taken up promptly and destroyed by the cells, the individual, through the activity of his cells, has received protection from a mischievous enemy.

Interesting and suggestive experiments have been done by Almquist that indicate that phagocytosis is not dependent so much upon the activity of the cell as upon its structure. He found that phagocytosis, or at least the incorporation of bacteria by the leukocytes, was a phenomenon of dead as well as of living cells, and, therefore, might depend upon the penetrability of the cytoplasm for the bacteria. His experiment, however, does not explain the vital phenomenon of chemotaxis, for he compelled dead leukocytes to take up the bacteria by centrifugation, while in the pathologic processes accompanied by chemotaxis and phagocytosis, as we shall see later, there are a wholesale exodus of living leukocytes from the blood vessels and a general phagocytosis.

The cells of the human body are not nourished by phagocytosis and do not incorporate and digest their own nutrient. Instead of this, the most beautiful manifestation of division of labor gives them an ever-present, perfectly adapted, predigested pabulum upon which to nourish themselves, the preparation and distribution of the pabulum being the work of their fellows. From this source the cells reintegrate their worn-out substance and withdraw those materials out of which they elaborate the secretions and excretions of the body.

Irritability and **conductivity** are two closely associated phenomena. Chemical, electric, mechanical, photic, or thermal stimulation at once affects cells, whose irritability is shown by contraction. It is well exemplified in the case of the ameba, which, when stimulated, at once draws in its pseudopods and assumes the spherical form. The irritation is not followed by a local reaction. It is not a particular pseudopod of the ameba that is drawn in, but the irritation extends to every part of the cytoplasm by its inherent conductive powers, and all the pseudopods are withdrawn at once. It is by the manifestation of conductivity and contractility inherent in cells, and greatly specialized in some of the cells,—muscle fibers and nerve cells and fibers,—that many of the functions of the higher animal are made possible.

Reproduction.—The cells are capable of reproduction. By this is meant that they replace those of their kind which in the natural course of events wear out and die. In the early development of the body its cells grow rapidly in numbers through their inherent reproductive powers. In adult life the healthy animal is continually, though probably slowly, replacing its worn-out cells. Sometimes in disease certain of the cells take on a rapid and abnormal multiplication, which may terminate in profound tissue alterations, functional inabilities, and not infrequently in death.

The multiplication of the cells of the human body invariably takes place by division. Two kinds of cell division are described, the *direct* and the *indirect.* They differ in that the indirect form of cell division is preceded by a series of remarkable changes in the nucleus, which give it the name *karyokinesis* or *karyomitosis.*

Endogenous cell formation, by which cells are formed within other cells, is probably never seen in the human organism either in health or in disease. At one time giant cells were looked upon as mother cells, whose nuclei represented the incompletely developed offspring, but at the present time this theory is abandoned. Endogenous cell formation is seen in the low forms of life belonging to the sporozoa, and is well illustrated in the embryonal development of the coccidia of the rabbit, in which the adult organism transforms itself into a sporocyst containing a multitude of embryos.

Direct cell division is an infrequent mode of cellular multiplication that occurs chiefly in cells of the lymphoid variety. It is best observed in the leukocytes of the frog, kept in lymph or serum in a moist chamber, under the microscope.

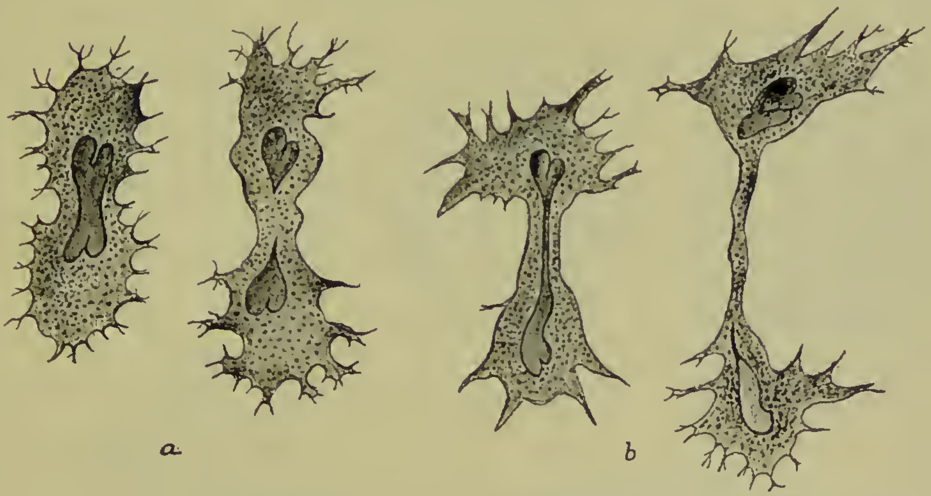

FIG. 53.—Direct division of lymphocytes of a frog (Arnold).

The cellular division proceeds without preliminaries, the first step consisting in a central constriction of the nucleus. The constriction becomes more and more marked and the halves more and more widely removed from one another, a bridge of nuclear substance connecting them. The cytoplasm next begins to show an increasing constriction at a position corresponding to the nuclear separation. The nucleus finally divides into two; ultimately the cytoplasm also divides and two cells exist in the place of one. In cases in which the cytoplasm fails to divide, multinuclear or giant cells are formed.

Indirect cell division (**karyokinesis** or **karyomitosis**) is characterized, as the term karyokinesis suggests, by peculiar preliminary changes in the nucleus, whose chemical constituents separate from one another with unusual distinctness, pass through a remarkable series of orderly transformations, and are permitted by the disappearance of the nuclear membrane to enter into a much closer relationship with the cytoplasm than would under normal conditions be possible. In describing the process, Hertwig finds it convenient to divide it into certain phases, which method may with advantage be here adopted.

First Phase.—The Preparation of the Nucleus for Division.—The nuclein or chromatin particles which have been distributed throughout the linin framework of the nucleus approximate one another and gradually unite to form a long, coiled thread. The nucleolus, if present, becomes gradually smaller and smaller and disappears. In the beginning of its formation the edges of this thread present a fuzzy appearance from the projecting irregularities of the chromatin particles entering into its composition, and as it becomes older the particles pack closely together and this effect is lost, the fibers becoming smooth. It is possible that only one thread exists in the nucleus, or it may be, as Hertwig and Rabl believe, several of them, all entering into the formation of the coil.

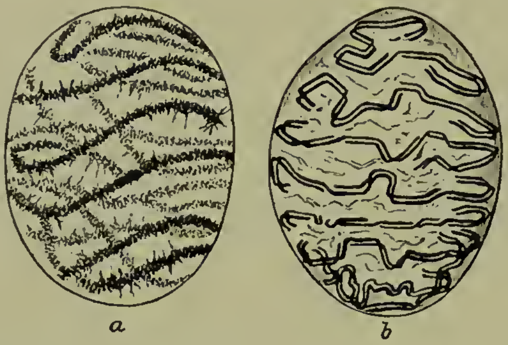

FIG. 54.—Nuclear changes in karyokinesis: *a*, Nucleus of spermatoblast of Salamandra maculata, with chromatin threads forming the first suggestion of a coil; *b*, close coil with disappearance of the fuzzy aspect and longitudinal cleavage of the threads (Hatschek).

During this stage it is obvious that the chromatin takes the stain much more energetically than usual. This is especially the case in sections stained by Gram's method, where the normal nuclei become completely decolorized by treatment with alcohol, while the dividing nuclei retain the stain.

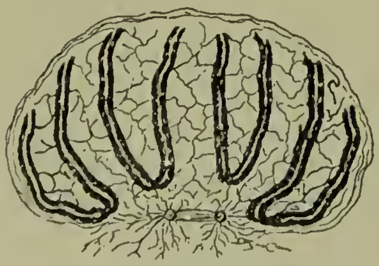

FIG. 55.—Diagrammatic appearance of the relation of the chromosomes to the centrosomes and primitive nuclear spindle (Flemming).

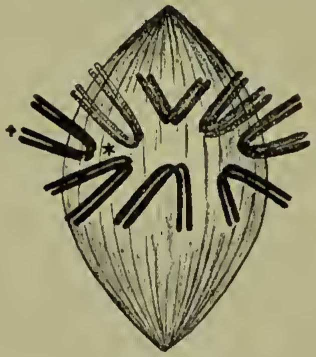

FIG. 56.—Diagrammatic representation of the nuclear spindle and of the arrangement of the double chromosomes in an equatorial plane preparatory to separation. This stage is called the mother star (Flemming).

Rabl found that there was always a peculiarity of arrangement during the formation of the coiled thread, by which a certain area, which he called the polar field, became the center about which the nuclear threads arranged themselves. A second polar field is found opposite that first formed.

While the nuclein is thus arranging itself in this coil, which some call the "*close coil*" or "*close skein*," the *polar body divides into two*, the halves becoming slightly removed from each other, but connecting by a number of extremely fine filaments which form the beginning of the nuclear spindle.

Second Phase.—Disappearance of the Nuclear Membrane and Division of the Chromosomes.—The nuclear membrane now gradually disappears and the nuclear substance becomes free to disseminate itself throughout the cytoplasm. The nuclear thread which has been forming its windings in a regular form, the angles radiating from the polar field, breaks up into fragments, the number of which is constant for the cells of each animal. In Salamandra maculata, which has been used by Flemming for his studies of karyokinesis, the number was 24, in man 16. Each fragment is known as a *chromosome* or nuclear segment. The chromosomes begin to assume a definite radiating form about the polar field, which moves toward the center of the cell, and the polar bodies gradually move apart, the filaments of the nuclear spindle elongating until it becomes a large and important element in the cell. At the poles the granules of the protoplasm also seem to be influenced, and some of them take on a radiating arrangement around the polar bodies.

The chromosomes now become thicker and shorter, and in the salamander form distinct V-shaped segments, which form a perfect equatorial ring about the axis of the spindle, their closed ends all directed toward the center. This stage is called by Flemming the "*mother star.*" It is succeeded by one of the most interesting phenomena of the whole series, which consists of a longitudinal splitting of every chromosome, so that it now consists of two parallel threads. This division of the chromosomes seems to be a constant phenomenon of karyokinesis.

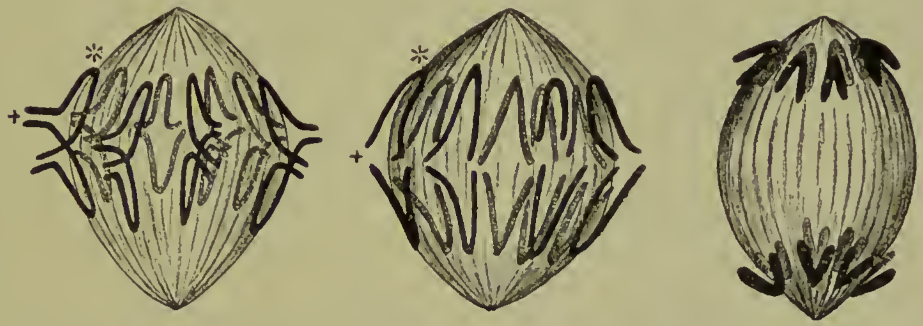

FIG. 57.—Diagrammatic representation of the separation of the chromosomes, which are attracted toward opposite poles of the nuclear spindle, about which they gather to form the "daughter stars" (Flemming).

Third Phase.—Separation of the Chromosomes and the Formation of Daughter Stars.—The chromosomes which have undergone the longitudinal cleavage retain their original position, the angle being directed toward the long axis of the nuclear spindle. Beginning at the apices of the angles, the two fragments now begin to move in opposite directions, the angles becoming widely separated from one another before the ends move. The result of the movement is the division of the nuclein into two portions, consisting of an equal number of equal-sized chromosomes, which now arrange themselves radially about the poles of the nucleus, and so form what Flemming has called the "*daughter stars*" or *amphiaster*.

Fourth Phase.—The Transformation of each Daughter Star into a Perfect Nucleus.—The arrangement of the chromosomes about the poles is at first typical and exactly resembles the mother star. The appearance lasts but a short time, however, then the chromosomes are observed to draw closer together, lose the definiteness of their arrangement, become more crooked than heretofore, and soon to develop a rough, notched surface with bristling projections, exactly as seen in the chromatic filament of the parent nucleus during the formation of the loose coil. Indeed, the steps in the perfection of the nucleus are but the reverse order of the original series. About each future nucleus a delicate membrane now forms, the radiating arrangements disappear, and in a short time it is impossible to distinguish the polar bodies or nuclear spindle. Each young nucleus at first appears somewhat flattened, and shows a saucer-like depression where the centrosome or polar body was situated. What becomes of the polar bodies is unknown; Rabl believes that they remain inclosed in the newly formed nuclei. The nuclei gradually absorb fluid from the cytoplasm of the cell, swell into a rounded form, and finally present the normal size and appearance, with the usual granular and fibrillar arrangement of nuclein. In cells normally provided with nucleoli these bodies finally make their appearance, their origin remaining unknown.

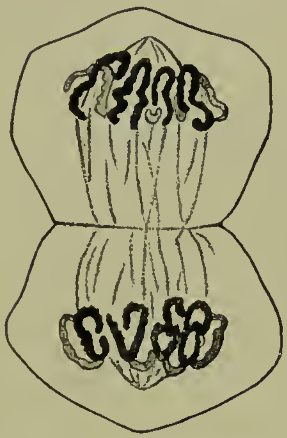

FIG. 58.—Segmentation of the cytoplasm, and the chromosomes equally divided, about to form new nuclei in the new cells (Flemming).

The division of the cytoplasm and the actual separation of the two cells occur during the fourth phase of the karyokinetic process. It begins by the formation of a circumferential, equatorial constriction which corresponds to a transverse plane perpendicular to the long axis. The constriction becomes deeper and deeper, usually progressing more rapidly at one side than at the other, and about the time of the disappearance of the nuclear spindle completely divides the cytoplasm, with the formation of two cells.

The physiology of the cell is complicated. In general terms it may be said that every cell manifests the four cardinal physiologic functions of animal life—nutrition, reproduction, conductivity, and irritability.

CHAPTER VI.

RETROGRESSIVE TISSUE CHANGES.

DISORDERS OF GROWTH AND NUTRITION.

INADEQUATE GROWTH.

As the result of embryonal accidents, members, organs, or tissues may entirely fail to develop. More commonly a partial or incomplete development is observed. To the former condition the term aplasia, to the latter hypoplasia, is applied. Both conditions have been described as *atelciosis*—not attaining perfection.

Aplasia or, as it is sometimes called, agenesis is total failure of development. If the missing part be important and its absence attended by an obvious defect of structure, the individual is properly classed among the monsters. The most exaggerated illustrations of the condition are the acardiac and acephalic monsters, in one of whom the body, in the other the head, fails to develop. Usually it is organs of minor importance that are absent.

Hypoplasia is incomplete development. It is more frequent than aplasia, and depends upon abnormal conditions operating upon the growing individual at any time before adult size is attained. Aplasia usually depends upon conditions arising during the first weeks or months of embryonal existence; hypoplasia may depend upon conditions arising as late as, or even later than, puberty. The hypoplastic part resembles the normal part, as a rule, but is smaller and less nearly perfect in structure.

Etiology.—Many causes, unfortunately for the most part obscure, lead to hypoplasia. Chief among them are imperfect nutrition and imperfect innervation.

If the nutrition of the entire body be imperfect, the whole body will of necessity suffer and its development be impeded. If this condition be maintained and the individual live in spite of it, the full size is not attained, but a stunted or diminutive being known as a *dwarf* is the result. Dwarfs may occur in spite of what seem to be the best nutritional conditions, but in the physiology of such cases there is probably some hidden error of nutrition or metabolism upon which the condition depends. Children who are to become dwarfs may be born of natural size and appearance, or may be born far below the normal size. They may be the offspring of normal parents, and may themselves be parents of children that develop properly. An interesting description of some noted dwarfs can be found in Gould and Pyle's *Anomalies and Curiosities of Medicine.* The small stature of some of the noted dwarfs is remarkable, Buffon mentioning dwarfs 24, 21, and 18 inches tall, and describes one who at the age of thirty-seven years measured only 16 inches in height.

Dwarfs, for the most part, show marked indications of rachitis with deformity of the bones, and thus confirm the opinion that their small stature depends upon defects of nutrition. They are nearly always ugly of feature and markedly disproportionate, though there are numerous exceptions to this rule. Intellectually the majority of them are bright, though the cretins (*q. v.*) are idiotic.

If the nutrition of a member be impeded, as by the loose coils of the umbilical cord about an arm or leg of the fetus *in utero*, the loss of nutrition entails imperfect development or hypoplasia of the member. The binding of the feet of Chinese girls interferes with the nutrition and growth of the part pressed upon and hypoplasia results.

Hypoplasia resulting from defective innervation is seen in the anterior poliomyelitis of children, whose limbs no longer grow after the nerve cells supplying the motor and trophic influences have been destroyed.

Hypoplasia may remain unexplained in cases of diminutive kidney, infantile genital organs, microcephalia, microgyria, and other local defects.

MALNUTRITION.

The tissues of the body may suffer malnutrition through the abnormal quantity or abnormal quality of the pabulum they receive. Abnormally great and abnormally small quantities of nutriment may injure the cells. In the order of pathologic importance the changes resulting from malnutrition are necrobiosis, atrophy, necrosis, and death.

NECROBIOSIS.

Necrobiosis is the molecular death of tissue. The term was first employed by Virchow to describe pathologic conditions in which the cells of a still living tissue were in a condition of compromised vitality depending upon malnutrition.

It is customary to speak of the necrobioses as *degeneration*, this term indicating any retrogressive change in the cells. Two chief forms of degeneration are described: *infiltration*, in which some new substance is added to the cell, and *metamorphosis*, in which the cell substance is transformed into some new substance and so destroyed.

The infiltrations not being essentially characterized by any alteration of the cytoplasm, are for the most part less serious than the metamorphoses. The former recover, the latter cannot.

The degenerations are, however, so numerous, so lacking in distinctive features, and at present so imperfectly understood, that it is frequently impossible to decide whether a certain form of disease is an infiltration or a metamorphosis.

Though imperfect, the following is suggested as a convenient method of classifying the cellular changes:

1. Conditions resulting from the absorption and retention of harmless materials conveyed to the cells by the circulating tissue juices: Fatty, calcareous, glycogenic, serous, and pigmentary infiltration.

2. Conditions resulting from the absorption of materials which exert a marked destructive effect upon the cells when brought to them through the tissue juices: Cloudy swelling and fatty metamorphosis.

3. Conditions depending upon the transformation of the cell substance into a pathologic material:

(*a*) The change probably being brought about by the activity of some ferment: Amyloid disease and hyaline degeneration.

(*b*) The change probably being more simple: Mucoid and colloid metamorphosis and pigmentary degeneration.

FATTY INFILTRATION.

Fatty infiltration is the assumption and retention of fats by the cells. It is a common physiologic phenomenon, and becomes pathologic only when it occurs in unusual tissues or in excessive degree. Under normal conditions fats are deposited in the subcutaneous cellular tissues, the subperitoneal tissues, the subpericardial tissues, and in the fasciæ. After meals rich in fats some globules may appear in the cells of the liver. The increase in fat deposition may be common to the entire body, causing the condition described as *obesity* or *polysarcia* (*q. v.*), or may be limited to certain organs.

The most typical example of local fatty accumulation is seen in lipoma (*q. v.*), although a local fatty infiltration occurs in the liver in pulmonary tuberculosis with marked wasting of the body.

Etiology.—Fatty infiltration may depend upon *hereditary* influences, as in obese families. It may also depend upon *excessive nutrition*, it being an everyday observation that well-fed persons are usually stouter than the poorly fed. Certain *digestive disorders* associated with excessive appetite predispose to fatty infiltration by the hypernutrition that is induced. The use of *alcohol* in quantities and dilutions favoring the digestion of food increases nutrition and so predisposes to it. *Anemia* with insufficient oxygenation of the blood and diminished combustion of fats in the body may be accompanied by fatty accumulations in the subcutaneous tissues. Certain *marasmic diseases*, such as pulmonary tuberculosis, are accompanied by fatty infiltration of the cells of the liver at the same time that wasting occurs elsewhere. *Lack of exercise*, by diminishing the combustion processes of the body, favors fatty accumulation.

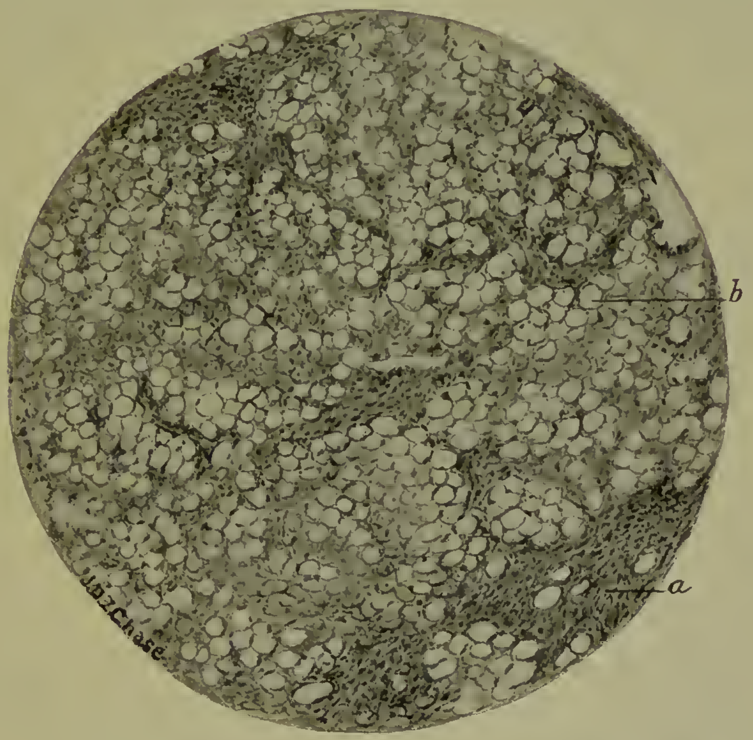

FIG. 59.—Fatty infiltration of the liver: *a*, Periportal connective tissue; *b*, fat drops in liver cells.

Seats of Occurrence.—Under physiologic conditions fat is deposited beneath the skin and serous membranes, in the fasciæ, and in the areolar connective tissue. Certain parts of the body invariably escape infiltration, no matter how exaggerated the condition, among these being the lips, eyelids, ears, alæ nasi, and sexual organs. Certain other parts, such as the palms of the hands and soles of the feet, are never without fatty cushions, no matter how emaciated the patient becomes.

Morbid Anatomy.—Fatty infiltration leads to a marked increase in size because of the presence of the fat. In human beings the fat, which consists of neutral palmitin, olein, and stearin, has a yellowish color similar to that of the fat of the ox. Fatty infiltrated tissues or organs are, therefore, enlarged and yellow. The fat is deposited in tissues containing few blood vessels, hence is usually quite anemic. In cutting or handling the fatty tissues the fingers and knife become soiled and greasy. The tissue is apt to be abnormally friable. If the fat is uniformly deposited in a tissue, it gives it a uniform yellow color. If irregularly deposited, the tissue will appear either streaked or mottled. A remarkable appearance characteristic of fatty infiltration is the "nutmeg" liver, caused by the most marked deposition of fat occurring about the periphery of the liver lobules.

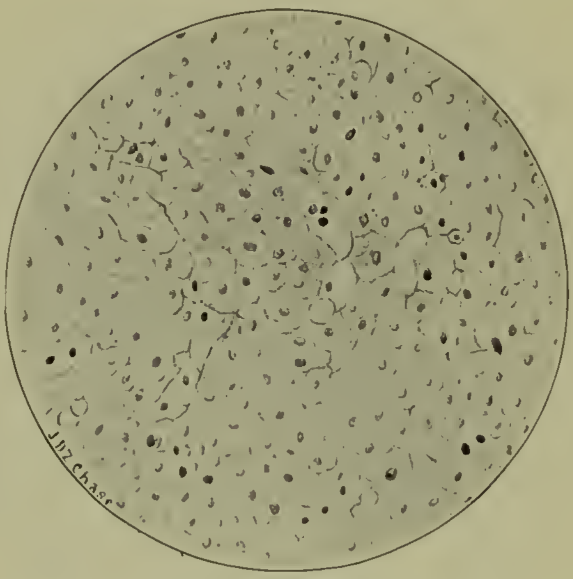

FIG. 60.—Fatty degeneration of the liver. Taken from a case of phosphorus-poisoning. The cells are indistinct and are filled with small deposits of fat. Oc. 2; ob. 9.

Pathologic Histology.—The fat is found, upon microscopic examination, to occur in the form of vesicles, which vary in size according to the tissue affected. In the adipose tissues the vesicles are very large, and when numerous are faceted by mutual pressure, so that they resemble a mass of bubbles. In lipoma the vesicles of fat are still larger and this appearance is more marked. It can with difficulty be determined that these fat vesicles are inclosed within cell envelopes. Indeed, the appearance of many of them suggests that they lie free in the spaces of the areolar tissue. This is, however, not the case.

The relation of fat droplet to cell is better observed in fatty infiltration of the liver, where the entire process can be traced and studied. The infiltration begins with the formation of a small droplet in the cell. This gradually grows larger, the nucleus being pushed aside, until the cytoplasm forms a mere capsule about it, and the nucleus is crowded aside and flattened in consequence. At this stage the microscopic appearance of the cell is compared to a "seal ring," the nucleus representing the seal and the attenuated cytoplasm the ring.

Microchemistry.—The appearance of fat is usually sufficient to enable one to recognize it without a test. It is soluble in ether, absolute alcohol, benzol, and xylol; insoluble in water, acids, and alkalies. It stains black with a 1 per cent. solution of osmic acid, and scarlet red with a solution of Sudan III.

In microscopic sections which have been prepared in the usual manner by embedding in celloidin or paraffin, and have been cleared in xylol after dehydrating in strong alcohol, the fat is no longer present, as a rule, though the spaces it once occupied are all obvious enough. Occasional spicular and hedge-hog crystals of fats remain in the fat spaces regardless of the method of preparation.

Postmortem changes of interest sometimes occur in fat bodies that are interred in damp soil, the most important being the transformation of the fats to a waxy substance known as *adipocere.* As bodies in which adipocere forms are usually well preserved, its formation accounts for certain so-called "petrified bodies."

GLYCOGENIC INFILTRATION.

This is the accumulation of glycogen in the cells. It occurs in the epithelial cells of the liver and kidney, and at times in the muscles and in embryonal tissues, in small quantities during health, hence in limited extent cannot be regarded as pathologic. In certain diseased states, however, its amount becomes excessive and hastens the dissolution of the cells.

The source of the glycogen is somewhat obscure. It is a carbohydrate, but seems to be elaborated both from carbohydrate and proteid substances. It is readily converted into dextrose, and it is probably that form in which sugar is stored in the tissues until ready for consumption.

In pathologic conditions it appears in small quantities in the blood and pus, and in diabetes in the cells of the liver and kidney in large amounts.

Etiology.—Pathologic glycogenic infiltration depends upon the inability of the individual properly to regulate the conversion and utilization of carbohydrates. It is most frequent in diabetes mellitus (*q. v.*). Small quantities of glycogen appear in the cells in certain inflammations, and in some of the neoplasms.

Morbid Anatomy.—Glycogenic infiltration produces no changes that can be recognized by naked-eye inspection.

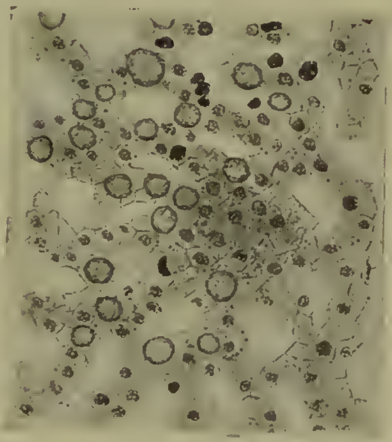

FIG. 61.—Glycogenic infiltration of the liver. × 300 (Hektoen).

Pathologic Histology.—The glycogen occurs in the form of clear, colorless, homogeneous droplets in the cells near the nuclei. They are usually small, although in diabetes, in the liver and kidney cells, they may be large. Sometimes they occur in the intercellular substance.

Chemistry.—Glycogen is soluble in water, but not in alcohol, chloroform, ether, xylol, or benzol. In order to detect its presence the tissue must be hardened in pure alcohol and passed through reagents containing no water. It is turned a port-wine color by a mixture of 4 parts of absolute alcohol and 1 part of tincture of iodin, this reaction being employed for its detection.

SEROUS INFILTRATION.

Serous infiltration is dropsy or edema of the cells. It is also called "hydrops" and "hydropic degeneration." It affects cells of all kinds, but is best observed in the epithelial cells.

Etiology.—The condition is likely to follow dropsy or edema of the intercellular tissue arising during anasarca, and from local edema from inflammation, hyperemia, etc. It also occurs sometimes in the cells of tumors, most likely in consequence of local disturbances of circulation.

The occurrence of cellular edema probably depends entirely upon the excessive quantity of fluid with which they are in contact and which they imbibe. It may be, however, that the tonic condition of the cytoplasm is impaired through nutritional disturbances, and the cell thus stimulated to take up the fluids.

Morbid Anatomy.—Dropsy of the cells cannot be recognized with the naked eye, though a part in which dropsical cells are present is usually enlarged, soft, moist, and boggy.

Pathologic Histology.—The affected cells are large—sometimes many times the normal size—and are filled with large and small transparent and colorless vacuoles. The vacuoles occur both in cytoplasm and nucleus and may cause destruction of the cell. The quantity of water that can be taken up by cytoplasm without injury is, however, surprising, some vegetable cells being able to take up sufficient to increase their volume a hundredfold. When sections of edematous tissue are stained, a faint homogeneous tinge of the entire structure suggests that some of the chromatin has been dissolved and pervades the cytoplasm.

Chemistry.—The absorbed fluid consists essentially of water, but probably contains some salts and proteids.

Pathologic Physiology.—Except in extreme cases the cells seem able to continue their function without inconvenience. Some of the cells show such marked nuclear changes, however, that their vitality would seem of necessity to be compromised.

CALCAREOUS INFILTRATION.

Calcareous infiltration, calcification, mineralization, or petrifaction of tissue consists in the deposit of lime salts in and between the tissue cells. Etymologically considered the term should apply only to deposits of lime salts, but custom has made it convenient to speak of the uratic-tissue deposits of gout under the same heading. It is correct to speak of *ossification* only when true osseous tissue is formed.

Etiology.—Leaving the uratic deposit of gout for future consideration, it may be said, in general, that calcification of tissue occurs in consequence of deficiency of oxygen and excess of carbon dioxid in the tissue juices, by which the carbonates and phosphates of magnesium and calcium are precipitated. This inadequate oxygenation occurs locally and is dependent in nearly all cases upon circulatory disturbances. As specially predisposing to the condition the following may be mentioned:

1. **Imperfect Circulation.**—(*a*) *Senility*, because of the arteriosclerosis usually accompanying it, is an extremely fertile source of calcifications such as are found in the vessels themselves and upon the valves of the heart.

(*b*) *Abnormally constructed tissues*, such as result from inflammatory processes and neoplasms are usually poorly supplied with blood vessels, present many indications of imperfect circulation, and are apt to calcify. For this reason old encapsulated and inspissated collections of pus, cheesy tubercles, cicatrized gummata, deposits of fibroid tissue upon the surfaces of the pleura and pericardium, spleen, and other organs commonly are found in a mineralized state. Tumors, especially of the dense tissues, and particularly fibroids of the uterus, are very badly nourished and subject both to necrosis and calcification.

(*c*) *Dead tissues*, such as are observed in thrombi, and dead fetuses escaped from a ruptured tubal pregnancy, are particularly prone to absorb lime salts.

2. **Special diseases** associated with irregularity in the distribution of the mineral elements, such as rickets, osteomalacia, gout, etc., may be associated with deposition of the lime salts.

3. **Intoxication** with bichlorid of mercury, bismuth, and aloin brings about absorption of the lime salts from the bones and their redistribution or elimination. The peculiar phenomenon known to the Germans as "Kalkmetastase" is observed in bichlorid of mercury poisoning. The lime salts are rapidly absorbed from the bones and eliminated with the urine, and, reaching the kidney more rapidly than it is possible to eliminate them, accumulate in that organ. This phenomenon occurring in intoxication suggests that the peculiar diseases known as osteomalacia and osteopsathyrosis are associated with some similar form of intoxication not yet understood.

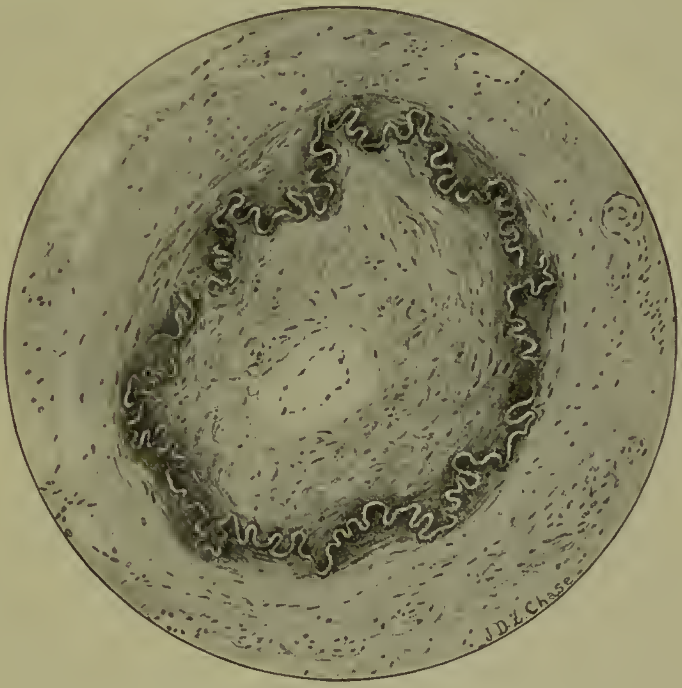

FIG. 62.—Calcareous infiltration of the wall of a small artery from the wall of a gumma of the liver. In addition to the calcification that has occurred in the media contiguous to the fenestrated elastic layer, there is marked syphilitic endarteritis with great reduction in the caliber of the vessel from proliferation of the subendothelial tissue of the intima. Zeiss, Oc. 2; ob. D. D.

Morbid Anatomy.—When the changes characterizing calcification are apparent to the naked eye, the tissues are hard and stony or friable and gritty. In solid tumors of dense tissue, such as uterine fibroids, the tissue may be too hard to cut with a knife and too gritty to saw readily. Increased weight usually accompanies the presence of the salts in the tissue. Cylindric tissues, such as blood vessels, may be transformed into veritable pipes—"pipe-stem arteries."

Upon the interior of blood vessels in the terminal stage of atheroma plates of calcareous material not unlike fish-scales are frequently found. In old abscesses and tubercles the lime salts may occur either as simple gritty matter or as concentrically deposited lamina about some central nucleus. In old thrombi and in inspissated fecal matter in the vermiform appendix the deposition of the lime may form actual stones (*phleboliths*, *enteroliths*), movable within the cavity in which they are formed. Upon fetuses retained in the abdominal cavity after escape from a tubal gestation by rupture the lime salts are deposited chiefly in the form of a superficial incrustation (*lithopedion*).

Pathologic Histology.—The calcareous material may be either amorphous or crystalline, and may be deposited in the cells or, as is more frequent, in the intercellular substance.

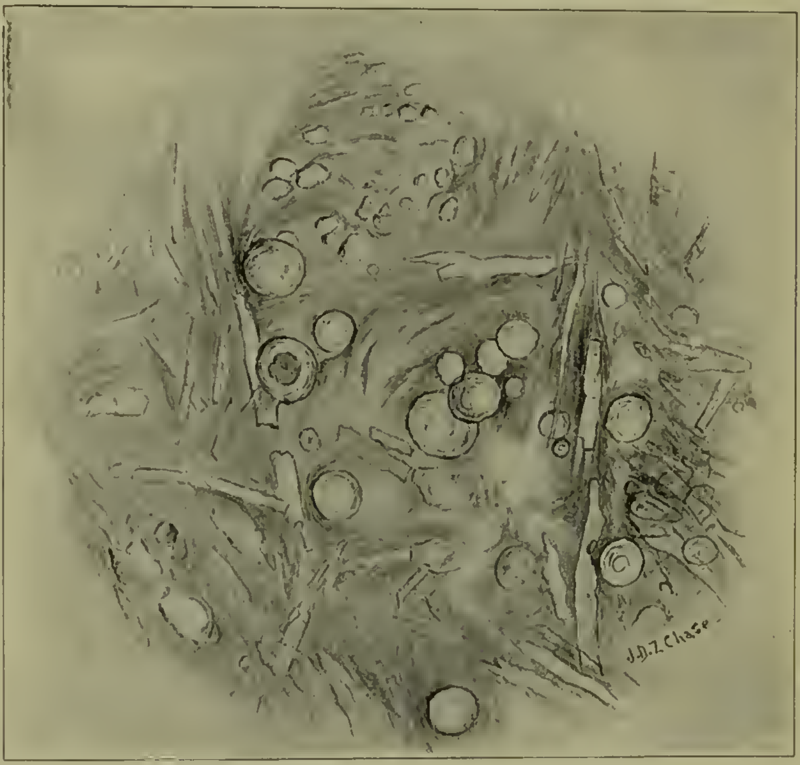

FIG. 63.—Psammoma—the matrix of the tumor.

1. **Cellular calcification** not infrequently occurs in diseased ganglionic cells of the nervous system and in the epithelial pearls of epithelioma of the skin. In both cases colorless mineral granules appear in a form corresponding to the cell outline, though the cell is destroyed.

2. **Intercellular calcification** may consist of a few amorphous granules deposited in the interstices of the denser tissues, such as the media of the arteries, the articular cartilages, cartilages of the ribs and larynx, etc. About such collections of granules the tissue has a very marked affinity for hematoxylin, and when stained with Delafield's hematoxylin the tissue in immediate contact with the calcareous salts assumes a blue-black color. Sometimes the color reaction can be detected when no calcareous material can be observed.

More advanced infiltration is characterized by granular material in the tissue; still more advanced degrees by mineral masses.

In the tumor of the nervous system known as *psammoma* the mineral deposit occurs in the form of small concentric spheres or laminated and spicular cylinders scattered throughout the matrix of the tumor.

Chemistry.—The lime salts are insoluble in water, ether, chloroform, alcohol, xylol, benzol, or other reagents usually employed in microscopic technic. They are soluble in dilute acids, especially in hydrochloric acid, with which they cause effervescence. It is by the disappearance of the salts when immersed in acid solutions that they can be differentiated from foreign mineral matter accidentally present in the body.

URATIC INFILTRATION.

Uratic infiltration, or deposits of sodium biurate in the tissues, is seen in *gout*. The salts are chiefly precipitated in the articular cartilages, though small rounded deposits sometimes occur in the skin and subcutaneous tissue and in the denser tissues about the affected joints. To such deposits the name *tophi* has been applied.

The uratic deposit as it occurs in tophi is usually impure, in that more or less admixture of lime and magnesium carbonate and phosphate is present.

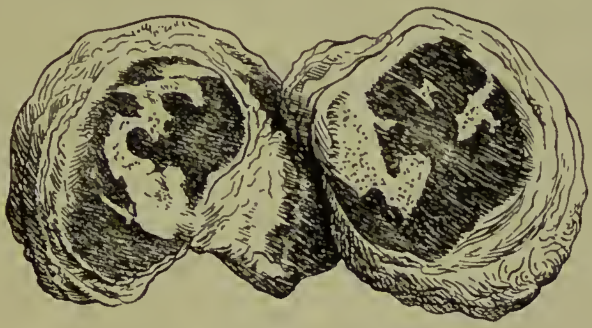

FIG. 64.—Arthritis uratica (Orth).

In this form the deposit is amorphous. In the joints, however, it is crystalline and spicular and affords visible evidence why the gouty joint should be so exquisitely painful when moved.

The tophi being superficial, frequently work their way to the surface, upon which the mineral deposit crumbles away like so much chalk.

Ossification, or the formation of bone in the tissues, occurs in a number of pathologic conditions.

1. **Neoplasms.**—Ossification occurs in benign tumors, such as uterine fibroids, and in malignant tumors, such as the ossifying sarcoma. The bone is usually somewhat atypical, although supplied with lacunæ and canaliculi, and of laminated structure. The tissue may be quite dense, though usually spongy.

2. **Myositis Ossificans.**—This is a peculiar disease in which bony deposits are formed in the muscular tissues. It is supposed to depend upon chronic irritation of muscles subjected to frequent mild trauma, such as may be experienced in military exercises and horseback-riding. Such lesions are described by the Germans as *Reitknochen* and *Exercirknochen*.

3. **Senile Arteritis.**—In the disease of the middle coat of arteries which so commonly accompanies senility the calcification may take the form of ossification. In disease of the intima bone is very rarely formed. The valves of the heart rarely contain bony formations.

4. **Osteophytes** are well-defined bony masses formed in unnatural positions. They can scarcely be classed as tumors, as they occur in normal structures, such as the falx cerebri, falx cerebelli, tentorium cerebelli, etc. They nearly always conform to the shape of the respective membranes in which they occur, and appear as thin, translucent plates.

Calculi are mineral concretions formed in cavities of the body by precipitation from its fluids. They form in the urinary bladder, gall-bladder, intestine, pelvis of the kidney, etc., and rarely in the nose, bronchi, ear, urethra, etc., by incrustation of foreign bodies. (The calculi of particular regions will be separately discussed in connection with the Special Pathology of those regions.)

Extraneous mineralization or **pneumonokoniosis** is the retention in the body of certain mineral substances which enter it with the inspired air, and are not formed by its own metabolic processes. It is the result of "*dust inhalation.*"

1. **Anthracosis,** from which all human beings suffer more or less, results from the inhalation of soot and coal-dust and its retention in the lungs, which, in consequence, appear irregularly mottled with black.

2. **Siderosis** results from the inhalation of iron filings or grindings, which impart a reddish-brown color to the lungs.

3. **Chalicosis** depends upon inhaled grit, lime, ground oyster shells, etc.

4. **Kaolinosis** is caused by the inhalation of clay, and is seen in potters, sculptors, and others.

Anthracosis is common and almost universal, but the other forms are rare. All forms of pneumonokoniosis are of little interest or importance when of mild grade, but become of interest when severe enough to lead to the pulmonary indurations known as "miner's consumption," a misnomer, for the lung, instead of being consumed, becomes indurated and fibroid.

When dusts are inhaled, the coarser particles are filtered out of the air by the cilia of the nostrils. Other particles are precipitated against the surfaces of the nose, pharynx, larynx, trachea, and bronchi and are retained, gradually being returned to the outer world by the action of the lashing cilia, ascending secretions, and effects of cough.

Some of the particles, however, reach the air cells, where they occasion a mild catarrh with some desquamation of epithelium and the exudation of some leukocytes. The dust particles are taken up by both the alveolar epithelium and the leukocytes, some reaching the expectoration, while many of them are carried into the interstitial tissue of the lung, to be deposited in endothelial and connective-tissue cells, others being carried to the bronchial lymph nodes, where they are permanently retained.

The dust particles in the air cells cause mild alveolar catarrh, so that the affected individual coughs; the presence of the particles in the interstitial tissue of the lung predisposes to induration by exciting proliferation of the connective-tissue cells and fibers, and the lung loses its elasticity. The coal-dust in the bronchial glands causes them to become enormously enlarged and softened, with occasional ulceration and erosion of the contiguous veins, through which the softened contents enter the circulation and find their way to remote parts of the body. Thus, in some severe cases of anthracosis, coal-dust has been found in the spleen, liver, kidneys, and nervous system.

PIGMENTARY INFILTRATION.

Pigmentary infiltration is the addition of pigment to a tissue. With the exception of the metabolic pigment *melanin*, which is produced by the cells, and which will be considered under another heading, all the pigments found in the body are direct derivatives of hemoglobin, the coloring-matter of the blood. In its normal transformation, hemoglobin becomes converted into bilirubin, the coloring-matter of the bile, which in the intestine becomes hydrobilirubin, and ultimately stercobilin, which imparts the brown color to the feces, and urobilin, which, being absorbed from the intestine and excreted by the kidney, gives the urine its amber color. The pigments that infiltrate the tissues thus come either from the blood or from the bile, and can be described as hematogenous and hepatogenous.

I. **Hematogenous Pigments.**—Of these pigments, three are of importance: hemoglobin, hemosiderin, and hematoidin.

1. **Hemoglobin** is found under normal conditions in the erythrocytes only. It is a dark-red, amorphous substance containing iron, soluble in water and solutions of alkalies; insoluble in alcohol, ether, and chloroform. *Almèn's test* for hemoglobin is the common medicolegal test for determining blood stains. It is performed by the addition to a solution of the hemoglobin or dissolved blood of a few drops of a freshly made tincture of guaiac, followed by an ethereal solution of hydrogen dioxid. The guaiac causes the solution to become milky white in color, the hydrogen dioxid turning it a rich blue. Hemoglobin, or dried blood containing it, when mixed with sodium chlorid and acetic acid is transformed into rhombic crystals of a brownish color (*hemin*).

In rapid hemolysis, such as is observed in chlorate of potassium and nitrobenzol intoxications, as well as in several of the infectious diseases, the hemoglobin, being liberated from the corpuscles, is dissolved in the plasma, to which it imparts a deep-red color. In such cases the tissues become stained by the plasma and appear redder than normal.

The transformation of hemoglobin into bilirubin in the liver is no doubt accelerated in such cases; still some of the hemoglobin reaches the kidneys and is immediately eliminated in an unchanged condition (*hemoglobinuria*).

The staining of the tissues resulting from hemoglobin is diffuse and is unaccompanied by any microscopic change.

When hemoglobin escapes from dissolving corpuscles and infiltrates the tissues after death, a peculiar change is frequently observed in consequence of the combination of the iron of the hemoglobin with sulphureted hydrogen and the formation of ferrous sulphid, which is black.

The most common seat of this change is the inferior surface of the liver, where the hemoglobin is brought into proximity with sulphureted hydrogen gas contained within the contiguous intestine. The change is sometimes present a few hours after death; it is not known that it may not take place during life when sulphureted hydrogen gas is present in the intestine.

2. **Hemosiderin** is an amorphous pigment of a yellowish or brownish color, insoluble in water, alcohol, ether, chloroform, xylol, benzol, dilute acids or alkalies. It contains iron, and turns blue when acted upon with a solution of chemically pure ferrocyanid of potassium and dilute hydrochloric acid. Ammonium sulphid turns it black.

Hemosiderin is a common pigment in all hemorrhagic conditions, hemoglobin seeming to be transformed into hemosiderin when the corpuscles of the blood are slowly destroyed. In all petechiæ, ecchymoses, suffusions, hematomata, and other diseased conditions associated with interstitial hemorrhage, as well as in hyperemia and inflammation with diapedesis, this pigment is present. It occurs both in the cells and in the interstices of the tissue, always in the form of amorphous granules of rounded form and irregular size. The granules are readily seized upon by the leukocytes, and it may be largely through the activity of the scavenging cells that the insoluble or slowly soluble granules are eventually removed.

Hemosiderin is quite common in neoplasms because of interstitial hemorrhages occasioned by the irregularities of circulation in tumors and the imperfection of their blood vessels. Care must be exercised lest it be mistaken for melanin and the disposition of the neoplasm misjudged in consequence.

3. **Hematoidin** is a reddish-brown pigment that occurs in the form of rhombic crystals at the seat of old hemorrhages. Hematoidin is insoluble in water, alcohol, or ether, but is soluble in chloroform. It contains no iron, and it is thought to be a changed form of hemosiderin.

Hematoidin usually occurs in the crystalline form in the fluids contained in old hemorrhagic cysts of the brain. It may also occur in the corpora lutea of the ovary and in the liver. It is much less frequent in occurrence, and hence of much less importance, than hemosiderin.

II. **Hepatogenous Pigmentation.**—Hepatogenous or biliary pigmentation depends upon the absorption of bile and the discoloration of the tissues by bilirubin. It characterizes the condition known as *jaundice* or *icterus*. Bilirubin being soluble, like hemoglobin, pigments the tissues only so long as it is being absorbed into the blood; so soon as its elimination recommences it disappears from them.

Gmelin's test readily determines the pigment. It consists in placing a few drops of the fluid containing bilirubin upon a white plate and allowing a few drops of fuming nitric acid to come in contact with it. At the point of contact a play of colors can be observed.

In most cases the hepatogenous pigmentation occurs as a diffuse staining of the cells and intercellular substance. It may, however, when of long duration, result in the formation of greenish-yellow granules or rhombic crystals, either between or within the cells.

Nearly all cases of hepatogenous jaundice depend upon obstruction to the outflow of bile from the liver. (See Jaundice.) It is also said that excessive bile production in cases of rapid hemolysis, such as occurs in young infants and from various intoxications, as well as in certain hepatic disorders, such as acute yellow atrophy of the liver, may cause it.

III. **Metabolic pigmentation** or **melanosis** is the formation of melanin by the cells.

This is observed as a normal process in the pigmented cells of the choroid and retina of the eye, and in the hair, muscles, and skin. It occurs only in the epithelial cells in man, though in some of the lower animals (chameleons and other reptiles and lizards) there are mobile, presumably connective-tissue cells which, by their migrations under the stimulation of light, cause the skin to change color from time to time.

Melanin seems, therefore, to be the natural pigment of the tissues. Its chemistry is somewhat obscure. It is usually conceded that it contains sulphur, but little or no iron. It has a dark color, varying from yellowish brown to black. It is insoluble in water, alcohol, and ether; soluble in boiling alcohol, acids, and alkalies.

Macroscopically the presence of melanin imparts a yellowish, brownish, or blackish color to tissues containing it.

Microscopically the pigment is found in the form of fine and coarse amorphous yellowish, brownish, or blackish granules between the cells, in the cells, and in the nuclei of the cells.

The chief pathologic conditions under which melanin occurs are melanotic tumors (see Melanotic Sarcoma), Addison's disease, malaria, muscular degeneration, and certain skin affections.

1. **Tumors.**—The chief melanotic tumor is the *melanotic sarcoma* or *melanoma*. The pigment is formed in the cells and leads to their complete

destruction and dissolution, the outcome of the process seeming to be the transformation of the entire cell into pigment granules.

Pigmented tumors, for some reason not understood, are more apt to be rapidly metastatic and fatal than unpigmented tumors of the same kind.

2. **Addison's disease** (*q. v.*) is characterized by melanosis of the skin, especially of the face, neck, shoulders, and hands. In some cases there is a general bronzing of the whole skin, the color resembling that of the darker mulattoes; in other cases the skin is streaked and smeared so as to appear soiled. The condition develops insidiously, and seems, from its frequent association with them, to depend upon destructive diseases of the adrenal bodies.

3. **Malaria.**—In malaria the parasites seem to effect the transformation of the hemoglobin of the infected erythrocytes into melanin, which is discharged free into the blood as the parasites segment, and subsequently pigment the organs in which they collect. In very severe chronic cases of malaria most of the organs, including the brain, may show this pigmentation.

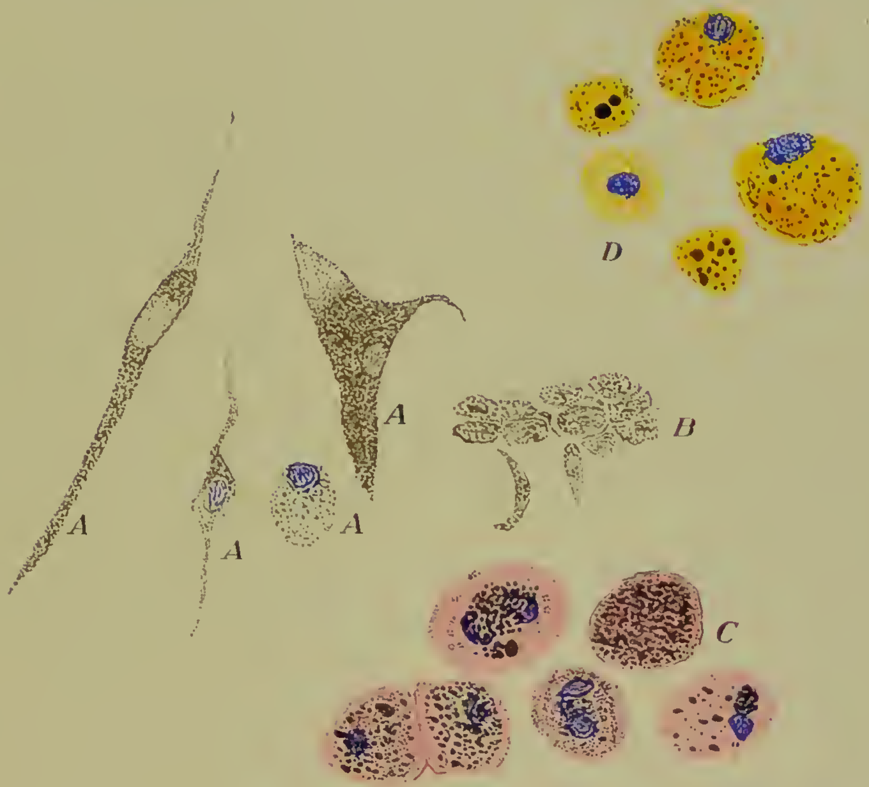

FIG. 65.—Various kinds of pigmented cells: *A, A, A, A*, Cells containing melanin, from a melanosarcoma of the choroid; *B*, pigmented cells from the skin in Addison's disease; *C*, cells filled with coal-dust in the alveoli of the lung; *D*, cells containing changed red cells and blood pigment in a lung the seat of passive congestion. × 650 (Hektoen).

4. **Muscular degenerations**, especially brown atrophy of the heart, may be accompanied by formation of melanin (?) granules in the muscular fibers. They usually appear near the muscle nuclei and are of a yellowish color.

5. The **skin affections** associated with pigmentary changes are:

(*a*) *Lentigo or Freckles.*—These are small brownish spots appearing upon the hands, face, and other parts of the body after exposure to the sun. Certain persons only, usually with fair complexions, are subject to this irregular pigmentation, the greater number experiencing regular bronzing of the exposed parts. In some persons freckles occur without exposure and are permanent. Ordinarily freckles, like sunburn, disappear when exposure is avoided.

(*b*) *Chloasma*, or irregular pigmented blotches upon the forehead and other parts of the face, are observed sometimes in pregnancy and in ovarian disease. They are of a yellowish-brown color, are indistinct at the edges, and form blotches and streaks.

(*c*) *Melanism.*—Extensive abnormal pigmentation of the skin, sometimes of congenital, sometimes of acquired, occurrence. Addison's disease is an acquired form of melanism. It also sometimes occurs in melanoma.

Having thus described the physiologic and pathologic conditions in which the pigment of the skin is increased, it may be well to mention a few important pathologic conditions in which the pigment of the skin is deficient.

1. *Vitiligo* or *leukoderma* is a congenital, rarely acquired, affection characterized by the occurrence of white spots upon the skin. The white spots are simply areas of local deficiency of the natural pigment. If hairs grow upon the affected area, they are pure white. Sunburn and exposure seem to have no bronzing effect upon the leukodermal patches, though the surrounding skin becomes dark. Leukoderma is most striking in the negro, in whom it is not infrequently acquired. The patches of vitiligo seem to be more frequent upon the head and face than elsewhere. The cause of the affection is not known, but it is supposed to depend upon some abnormality of trophic nervous influence.

2. *Albinism* is a congenital anomalous condition characterized by general deficiency of pigment. In this disease the skin and hair are perfectly white, the irides pink. The eyes are always unnaturally sensitive to light, which may depend upon deficiency of pigment. Nervous disorders seem to be associated with the condition; thus, nystagmus is very common in albinos. Albinism occurs in the lower animals as well as in man. It may be complete or partial, the eyes having a moderate degree of pigmentation and the hair a cream or tow color.

IV. **Extraneous Pigments.**—All pigments found in the body in health and disease are of its own manufacture, but it occasionally happens that foreign substances accidentally or intentionally introduced may also produce coloration. Of these may be mentioned *tattoo-marks*, *argyria*, and *anthracosis*.

1. **Tattoo-marks** depend upon the intentional introduction of india-ink, carmin, and other insoluble substances through needle pricks in the skin. By the pricking of the skin the pigments are deeply introduced, and are retained for years by the cells of the rete mucosum. Though many of the granules are gathered up by phagocytes and transported to the neighboring lymphatics, and others gradually brought to the surface and desquamated, enough remain to show the original design. Tattoo-marks fade slowly.

2. **Argyria** is the deposit of salts of silver in the skin, and results from the continuous medicinal use of nitrate of silver, depending upon the precipitation of chlorid of silver in the skin. The result of the deposit is that the skin assumes a grayish hue. The microscope shows the salt to be deposited in the form of small granules in the cells of the skin, kidneys, blood vessels, membranes of the brain, and sometimes in the serous membranes.

3. **Anthracosis** depends upon inhaled soot and coal-dust.

CLOUDY SWELLING.

Cloudy swelling, parenchymatous degeneration, or albuminous infiltration is a cellular disease characterized by the formation of an excessive number of albuminous granules at the expense of the cytoplasm. It may recover or may terminate in destruction of the cell. It is probably the most frequent and least serious of the cellular diseases.

Etiology.—Cloudy swelling occurs from a variety of causes whose effects are destructive to cell life, either by overstimulation or by depression ; thus:

Infectious diseases associated with toxemia are nearly always associated with cloudy swelling of the parenchymatous organs, especially those of elimination, such as the liver and kidneys.

Chemical substances, such as alcohol, phosphorus, arsenic, bichlorid of mercury, ether, chloroform, etc., perhaps also through the damage done in elimination, are accompanied by cloudy swelling of the cells of the liver and kidneys.

High temperatures occurring independently of infectious diseases, from nervous lesions, insolation, etc., may cause cloudy swelling, possibly through the elimination of leukomains.

The chief seats are the eliminative organs, especially the liver and kidneys, though other epithelial cells, as those of the salivary glands, pancreas, intestinal glands, and the cells of the heart muscle, may show it.

Morbid Anatomy.—The part affected is slightly enlarged, and is paler and less translucent than normal. The appearance is described by some as like that of a " cooked " organ. To the naked eye, there may be no visible alterations.

Pathologic Histology.—The affected cells are larger than normal and appear filled with minute colorless granules which obscure the nucleus. The nuclei are not altered at first, but as the disease advances take the stain badly, and eventually lose the staining quality altogether and are destroyed. The cells themselves undergo eventual dissolution and are resolved into a granular débris.

Fatty granules sometimes make their appearance among the albuminous granules. The distinctness of cellular outline is early lost. Badly degenerated cells may desquamate.

The presence of the granules is thought by some to express an exaggeration of functional activity. This is, however, probably an error, as normal cells are granular when at rest, not when functionating, and lose the granules when actively at work. Moreover, in the very conditions under which cloudy swelling occurs the functions are suppressed. The granules are, therefore, in all probability, entirely different both in origin and in chemistry from those of normal cells.

Chemistry.—The granules are insoluble in water, alcohol, ether, and chloroform, but are soluble in dilute acetic acid and in dilute alkalies. They are not stained by osmic acid, hence are not fat. They give the xanthoproteic reaction, which can be developed by immersing the tissue in dilute nitric acid, by which the granules are colored yellow, then adding ammonia, which changes them to orange red.

Termination.—Cloudy swelling may end in true parenchymatous degeneration with dissolution of the cell, or may recover. Although the cells are destroyed in groups, enough seem to escape to enable the tissue to regenerate in most cases. The parenchymatous degeneration is probably not in itself a cause of death.

FATTY METAMORPHOSIS.

Fatty metamorphosis is formation of fat at the expense of the cell substance. It is a common pathologic process, and differs from fatty infiltration in that the fat is not formed by synthesis out of materials brought to the cell and stored within it, but is formed by conversion of the cellular proteids, the cell being partially or completely destroyed.

The physiologic prototype is found in the formation of milk, the fat being formed at the expense of the glandular cells, certain parts of which are lost in the change. The fat thus formed is usually liberated in the form of fine granules, which remain suspended in the fluid, though during the early stages of lactation the cells or parts of cells themselves appear in the milk as *colostrum corpuscles.*

Under pathologic conditions fatty metamorphosis may affect epithelial, muscular, and connective-tissue cells, and may occur in the intercellular substance as well as in the cells. It is probably most frequent in the epithelial cells of the liver and kidney, in the heart muscle, and also occurs in the intima of atheromatous blood vessels.

Etiology.—Fatty metamorphosis occurs :

I. **From Malnutrition.**—1. *Senility.*—Changes in the blood-vessel walls are responsible for many local atrophic and necrotic changes in old age in which fatty metamorphosis plays an important part. Thus, when the rigid arterial walls compress the vasa vasorum, shutting off the nourishment of the larger vessels, fatty metamorphosis of the intima occurs in the form of *atheroma* (*q. v.*). Sclerosis and calcification of the coronary arteries may lead to atrophy or fatty metamorphosis of the cardiac muscle.

2. *Anemia.*—In rapid oligemia from severe hemorrhage the small blood vessels of certain parts of the body, notably of the retina, undergo fatty metamorphosis, rupture, permit blood to escape, and cause blindness.

In leukocythemia, pernicious anemia, and other conditions associated with markedly deficient oxidation of the tissues fatty metamorphosis may be widespread. Indeed, Osler says, in speaking of pernicious anemia, "In no other condition do we find such widespread fatty degeneration."

In local anemia or ischemia, such as is seen in tubercle, and other focal disorders, the caseation depends in part upon the malnutrition.

II. **From Intoxication.**—1. *Toxemia.*—Various poisons, such as phosphorus, chloroform, iodoform, arsenic, sulphuric acid, nitric acid, phloridzin, etc., are characterized by fatty metamorphosis of the tissues.

The poisons of the infectious micro-organisms often produce serious lesions of this kind, as in acute yellow atrophy of the liver, yellow fever, scarlatina, etc.

Sewer-gas poisoning, by diminishing the oxygenating power of the blood, is also a cause of fatty metamorphosis.

2. *Hyperthermia.*—Fever may lead to fatty changes in the tissues either because of associated intoxication or because of diminished oxygenating power of the blood.

Morbid Anatomy.—Tissues in which fatty metamorphosis has occurred are usually pale and anemic, grayish or yellowish in color, and reduced in volume. The appearance varies with the degree attained. It may be invisible to the naked eye, or a parenchymatous tissue like the cortex of the kidney may be gray or yellow. The liver in yellow fever presents a *boxwood* appearance, while that of acute yellow atrophy is lemon yellow. The diminished bulk depends upon loss of substance from absorption of some of the degenerated cellular tissue. The tissues are usually soft, flabby, and friable or lacerable. The knives and fingers become oily as the tissues are handled and incised. The atheromatous patches in the aorta form slightly projecting yellowish-gray plaques. The endocardium of a fatty heart appears grayish and opaque, while the heart muscle is pale or may be yellow. The degeneration is apt to occur irregularly, giving the tissues a streaked or mottled appearance. In the heart this is sometimes described as "tabby mottling." *Caseation* represents one form of extreme fatty change.

Pathologic Histology.—The cells in which fatty metamorphosis has taken place are characterized by the presence of a large number of minute droplets. It may require the use of osmic acid to determine their nature, though, as a rule, their size and refracting power are sufficient to enable their nature to be determined without chemical aid. The droplets rarely tend to coalesce. The nucleus early becomes diseased, stains poorly, and ultimately becomes destroyed. The entire cell may finally break up into granular fat. A cell which has become completely degenerated, but whose fatty globules still remain coherent, is frequently spoken of as a "compound granule cell." Leukocytes which are scavenging fatty tissue frequently load themselves with molecular fat, and are also called "compound granule cells" or "fatty granule cells." Such cells are not infrequent in the urine in the severe forms of parenchymatous nephritis, in the fluids of ovarian cysts, and in other fluids and juices from fatty degenerated parts.

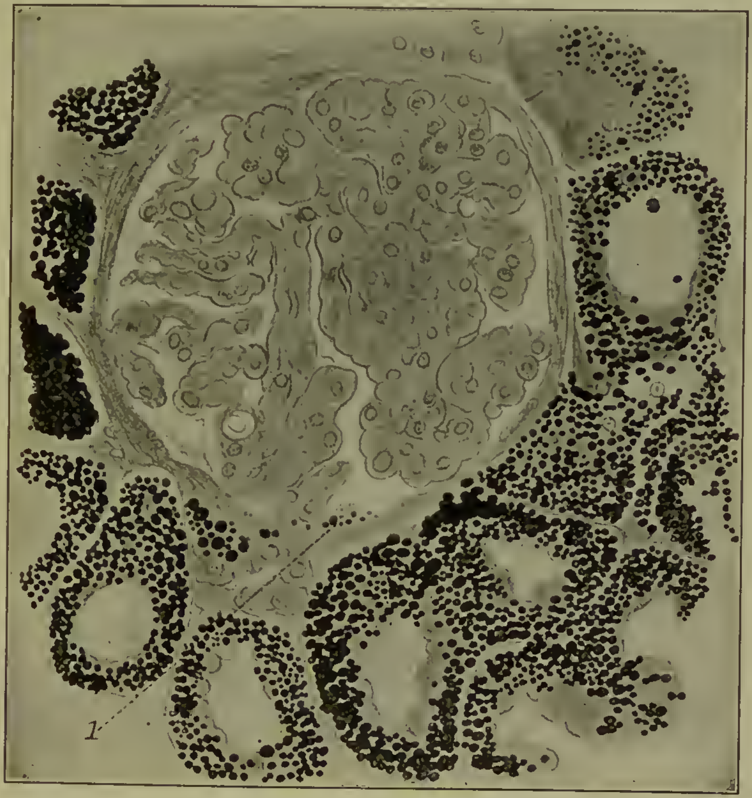

FIG. 66.—Fatty degeneration of the epithelium of the kidney (Dürck): 1, Desquamated cells with fatty changes in the capsular space.

Although it is usually possible to make a microscopic differentiation between fatty infiltration and fatty metamorphosis without much difficulty, there are tissues in which it may not be true; of these the liver is most important. In fatty infiltration of this organ several droplets may occur in the cell, while fatty metamorphosis may be complicated by coalescence of the droplets. Furthermore, as some fatty infiltration in the normal liver is frequent, the fatty metamorphosis of the infectious diseases and intoxications may be added to the infiltration, complicating the appearance.

When the infiltrated fat is to be absorbed to supply the needs of the economy the larger globules usually split up into smaller ones, this appearance sometimes suggesting metamorphosis instead of infiltration, and leading to confusion between a purely benign and a very destructive process.

Morbid Physiology.—The condition indicates lowered vitality and malnutrition, depending chiefly upon deficient oxidation or upon intoxication. It may be caused by anemia, hyperthermia, or trophic disturbances.

The chemistry of the process is obscure. It has been denied by some writers that proteids can change into fats.

Rosenfeld starved dogs until their own fats were consumed, then fed them upon sheep's tallow, which he found was stored up in the cellular tissues. After having a sufficient supply of sheep's tallow deposited in their tissues, he poisoned them with phloridzin, and observed 75 per cent. of the fat transferred to the liver, where it could be recognized chemically. He also found that when starved dogs were poisoned with phosphorus no fatty change occurred in the liver, because the "fat depots" were empty and no fat could be transferred there. Under these conditions the change in the liver is purely parenchymatous.

A. E. Taylor poisoned frogs with phosphorus, dried their bodies, pulverized them, and made chemical analyses to determine the relative proportions of proteid and fat present, comparing the results with similar analyses of normal frogs. No diminution of proteid or increase of fats was observed.

These experiments leave us in some doubt regarding the true nature of the process, but it is too soon to decide that the recognized opinions are erroneous.

Chemistry.—The fats formed are those normal to the body and the same that occur in fatty infiltration—*i. e.*, neutral palmitin, olein, and margarin. They are soluble in alcohol and ether, but not in water. They stain black with osmic acid, and red with Sudan III.

Termination.—It is not known how far the proteid transformation may progress before the vitality of the cell is destroyed. It seems probable that nearly all the affected cells die.

AMYLOID DISEASE.

Amyloid, albuminoid, waxy, lardaceous, or "bacony" disease is the infiltration of the tissues by an albuminoid substance not normal to the body. The amyloid substance is deposited in the intercellular substance of the connective tissues, not in the metabolic cells. It affects particularly the media and intima of the blood vessels, the framework and blood vessels of the liver, the framework and capillaries of the kidney, the Malpighian corpuscles of the spleen, the membrana propria of the mucous membranes, the blood and lymph channels of the lymphatic glands, and the heart and other muscles. The occurrence of extensive amyloid disease of an organ is usually associated with atrophy of its cells.

Etiology.—Amyloid disease is observed in chronic tuberculosis, syphilis, chronic suppuration, especially of the bones, chronic dysentery, and other wasting diseases. It is not known to occur in the cachexia of carcinoma. It is not so frequent as before modern surgery made possible the successful treatment of bone diseases.

Morbid Anatomy.—Amyloid disease may or may not be discoverable by the naked eye. In advanced cases the affected organs are enlarged, inelastic, pale, dense, and have their edges rounded and shape slightly altered. The larger organs can be readily pitted when pressed with the finger. When incised, the amyloid organ cuts normally. Its contained amyloid substance, if localized as in the "sago spleen," can be recognized as homogeneous, dense, translucent, and colorless areas. When diffuse, as in the liver, the organ appears unusually homogeneous.

Pathologic Histology.—The amyloid substance is formed in the tissue framework. It appears in the walls of the capillaries in the form of anuclear, homogeneous cylinders. In larger vessels it causes the walls to become thickened and the lumen diminished, the affected vessel walls being more translucent and homogeneous than normal. It also occurs in homogeneous, anuclear, irregular masses in the tissue, crowding out the parenchyma cells, which are apt to show fatty metamorphosis or atrophic changes.

The nutritional disturbances may cause associated fatty infiltration (especially in the liver in tuberculosis).

The amyloid material takes no stain and has no nuclei, so that there is a marked contrast between its homogeneity and indefiniteness and the cellular appearance of the healthy tissue.

In the kidney it affects first the capillary tufts of the glomeruli, slowly spreading until the entire tuft may be transformed to a waxy, homogeneous mass. Later it occurs in the interstitial tissue of the kidney.

In the spleen it affects the Malpighian corpuscles, which become transformed into rounded, homogeneous bodies, which have been compared to boiled sago grains, hence the name "sago spleen." Later it may spread in bands and streaks, until eventually scarcely any normal splenic cellular structure can be found.

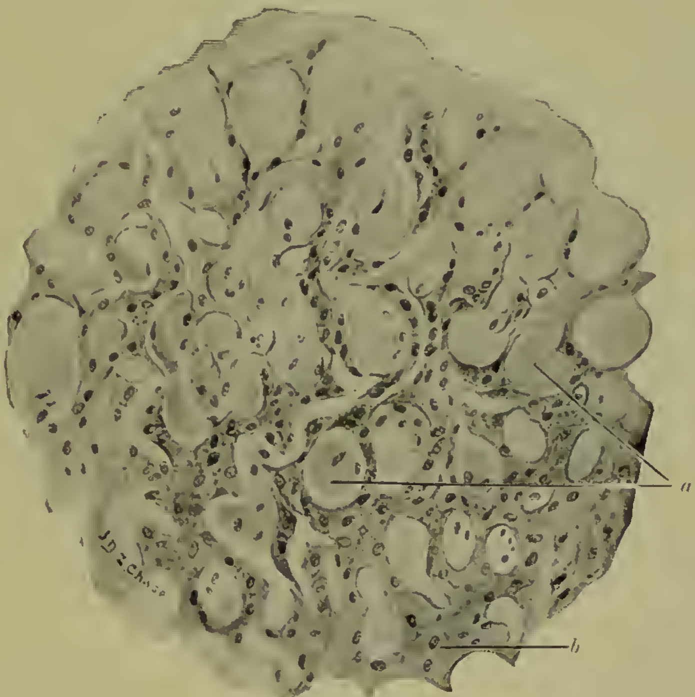

FIG. 67.—Amyloid degeneration of the liver: *a*, Amyloid masses; *b*, liver cells. Oc. 2; ob. 9.

In the liver the amyloid material is deposited irregularly in the zone intermediate between the periportal connective tissue and the central vein, the masses being sometimes large, sometimes small.

In the lymphatic nodes it usually attacks the capillary blood vessels and the walls of the lymph vessels.

In muscles it affects the perimysium and sarcolemma. When occurring in glandular organs and mucous membranes, the amyloid disease affects chiefly the membrana propria.

Pathologic Chemistry.—The source of the amyloid substance is obscure; it seems to depend upon an abnormal reaction between something in the tissue juices and something brought to them by the blood. No amyloid substance exists in the blood, though the blood is undoubtedly the source of the materials from which it is formed. Ziegler believes the amyloid substance to be an albuminate of the blood, which, because of the lowered metabolic power of the cells, is not properly converted into nutritive matter. Von Recklinghausen regards it as a cellular derivative which, when acted upon by the lymph, swells like mucus and forms masses in the tissue. Czerny believes the leukocytes to be the source. In many ways the amyloid substance resembles fibrin, and it is not impossible that its formation, like that of fibrin, depends upon the union of factors and ferments made possible through the presence or absence of certain salts.

The chemical conditions under which amyloid formation occurs are deficiency of potassium and the phosphates, combined with an excess of sodium and the chlorids. Amyloid substance is an albuminoid, insoluble in water, alcohol, ether, dilute acids or alkalies, chloroform, xylol, benzol, etc. It resists peptic digestion and withstands decomposition for a long time.

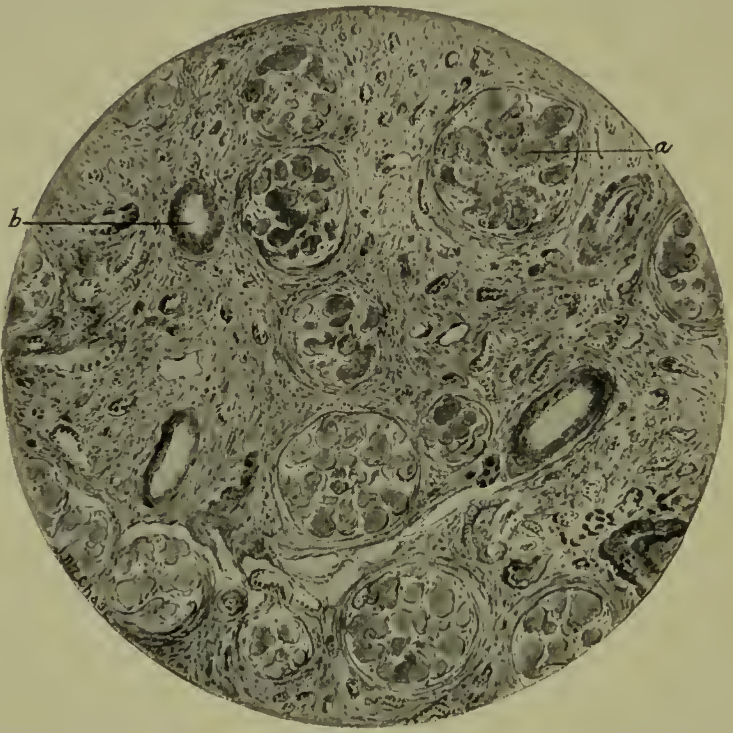

FIG. 68.—Amyloid degeneration of the kidney: *a*, Glomerule showing degeneration of its loops; *b*, vessel with degenerated walls. Zeiss. Oc. 2; ob. D. D.

Virchow observed that it had a peculiar affinity for iodin, and that when immersed in diluted Lugol's solution (iodin 1, potassium iodid 2, water 17) the amyloid substance becomes mahogany brown, contrasting with the normal tissue, which is yellow brown.

To make this test, a thin slice is cut from the amyloid organ, washed thoroughly in water to remove the blood, which becomes dark brown in iodin solutions, and immersed for a minute or two in the reagent, being subsequently thoroughly washed in water. The test can also be applied to microscopic sections. Fresh tissues react better than old alcoholic specimens.

Another peculiar reaction sometimes shown when the amyloid substance is present in large quantities is the "starch reaction." The tissue being first immersed in the iodin, and subsequently in dilute sulphuric acid, the amyloid substance becomes blue. This reaction is less commonly observed than the mahogany-brown color with Lugol's solution. It is most frequent in the amyloid bodies.

A third interesting reaction is developed by the use of aqueous solution of the anilin dyes. When amyloid substance is placed for a few minutes in a 5 per cent. aqueous solution of gentian-violet, washed in water, and examined in glycerin, the amyloid substance is pink, the normal tissues blue. Nearly all the anilin dyes tinge the amyloid substance some shade of red, while the normal tissue becomes green, violet, yellow, etc.

Course.—Cohnheim concluded that amyloid disease could become marked in a few months. Recovery from it is not known.

Amyloid bodies having nothing to do with amyloid disease are found in granulation tissue, in the lymphatic glands, in chronically inflamed tissues, in the prostate gland, and in the central nervous system. Their occurrence is not understood, but in most cases they seem to be associated with chronic irritation. The bodies are microscopic in size and are peculiarly laminated, like starch grains, hence are commonly called "*corpora amylacea.*" Their composition is different from amyloid in that they nearly always react with iodin and sulphuric acid with a blue color.

In the prostatic acini they appear to be formed by deposition of the secretion of the gland in successive layers; in the brain they may be formed from degenerated axis-cylinders; in lymph glands and granulation tissue they may originate from cells. They, therefore, are scarcely identical, though similar in appearance and in chemical reaction.

HYALINE METAMORPHOSIS.

Hyaline metamorphosis is the transformation of the cells into a hyaline substance resembling, but failing to give, the amyloid reaction. It chiefly affects the cells of the connective tissues, though it may also occur in epithelial and muscle cells. The process is not well understood, and different writers include quite different conditions under hyaline degeneration. Thus, von Recklinghausen, by whom it was first described, uses the term in a far broader sense than most pathologists, and makes it include the colloid metamorphosis of epithelial cells.

It affects both cells and intercellular substance, transforming the component tissue elements into homogeneous material with which iodin fails to produce reaction. Acid stains have more or less affinity for hyaline substance, the best reaction being observed in specimens colored by Van Giesen's method, with acid fuchsin and picric acid, which color it intensely red.

The hyaline substance sometimes occurs in the form of granules in and between the cells. The most familiar of these are the Russell's fuchsin bodies common in carcinoma, and at one time supposed to be parasites.

Larger hyaline masses are sometimes observed in the membranes of the brain and choroid plexuses, especially in tumors of these tissues, where they form laminated concentric bodies which are apt to become infiltrated with lime salts.

Hyaline degeneration is common in the connective tissue of the thyroid gland. It is common in atheroma of the blood vessels, affecting the subendothelial layers of the intima. It may be a general process affecting large numbers of the smaller vessels, transforming them into homogeneous cylinders whose walls are more or less nodular. Local hyaline degeneration of the walls of the blood vessels is frequent in sarcoma and forms the characteristic feature of cylindroma.

The blood vessels of the ovary, especially senile and chronically inflamed ovaries, frequently become hyaline.

The absorption of the corpus luteum is characterized by hyaline metamorphosis of the cells. It forms an important stage of muscle degeneration in senility and the infectious diseases, and has been observed in the heart muscle in so exaggerated a form that nearly all the tissue was affected. It is frequent in inflammatory lesions, and especially in the tissue round about tubercles.

It occasionally occurs in the capillaries of the lymphatic glands. Von Recklinghausen thought the process in old blood coagula sufficiently similar to be included in the hyaline changes. His definition is: "Hyalin is an albuminous body which colors instantly with eosin, carmin, picrocarmin, and acid fuchsin, appearing homogeneous and highly refractile; it is but slightly altered by acids, and is highly resistant to the action of alcohol, water, ammonia, and acids, in these particulars resembling amyloid, though failing to give the iodin reaction."

This conception makes it necessary to divide the hyaline substance into *epithelial hyalin*, which includes colloid and keratohyalin; *conjunctival hyalin*, arising from degeneration of the intercellular substance of the connective tissues and from the cells themselves by excretion of hyaline substance from them or transformation of their substance into hyaline substance; *blood hyalin*, which appears in thrombi; *exudation hyalin*, hyaline exudates appearing upon mucous or serous membranes, in the tubules of the kidney, in tubercle, etc., and *tissue-necrosis hyalin*.

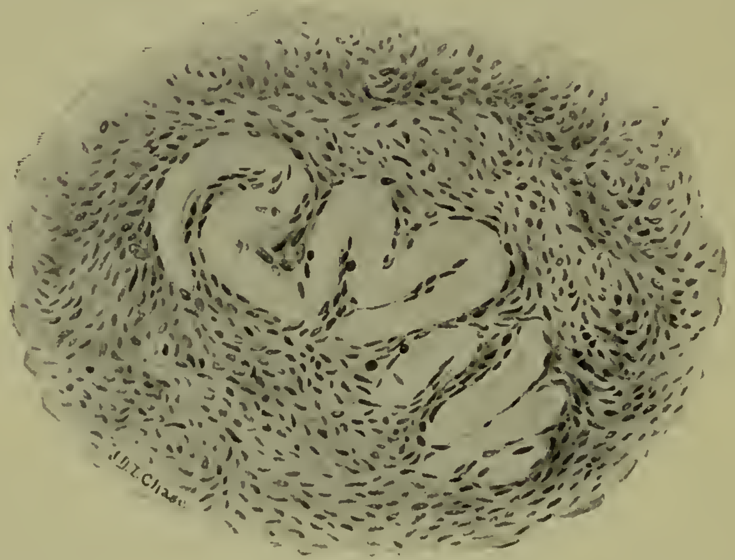

FIG. 69.—Hyaline degeneration of an ovarian capillary. Oc. 2; ob. 9.

Morbid Physiology.—The nature of the hyaline substance is unknown. It is thought to result from the action of some substance contained in the blood upon components of the cytoplasm, and is probably closely related to amyloid disease.

Morbid Anatomy.—When recognizable to the naked eye, the hyaline substance is firm, translucent, and homogeneous.

Pathologic Histology.—The hyaline substance is characterized by its homogeneous, glass-like appearance. The degenerated areas usually show lost differentiation of tissue elements. It is sometimes with difficulty differentiated from amyloid.

Etiology.—Nothing more is known of the origin of hyalin than that it depends upon malnutrition of the tissues.

It is seen in senility, chiefly upon the valves of the heart and in the walls of the great blood vessels; in infectious conditions, such as pseudomembranes, tubercles, gummata, etc. ; in tumors, such as cylindroma and psammoma, and in thrombi and emboli.

MUCOID METAMORPHOSIS.

Mucoid or myxomatous metamorphosis is the transformation of the cells and intercellular substance into a gelatinous, viscid substance rich in mucin.

I. **Mucoid Metamorphosis of the Cells.**—This is observed in certain epithelial cells of the mucous membranes and mucous glands, and takes place by the formation of goblet cells. The cells first show a vacuole in the cytoplasm, which becomes larger and larger, until the unattached end of the cell becomes greatly expanded by its presence and the cell goblet-shaped. The vacuole, which consists of mucus, is at length discharged from the cell, sometimes without injury to it, though the cell may be destroyed and detached together with its contained mucus.

Under pathologic conditions, such as arise in catarrhal inflammation of the mucous membranes, large numbers of cells may be thus affected and extensive desquamation occur.

II. **Mucoid metamorphosis of the intercellular substance** occurs in health in various parts of the body, such as the vitreous humor of the eye, the fringes of the synovial membranes, and the jelly of Wharton of the umbilical cord. It is a common pathologic process in neoplasms, specific infectious diseases (gumma, etc.), and in diseases of the bones and cartilages.

Etiology.—Mucoid metamorphosis of the epithelial cells of the mucous membranes occurs in all forms of catarrhal inflammation, in various cysts with epithelial acini, and in the cells of carcinomata. Mucoid metamorphosis of the intercellular substance is observed both in epithelial and connective-tissue tumors, in myxedema, and in certain inflammatory formations, such as gumma.

Morbid Anatomy.—The formation of an excessive quantity of mucus in catarrhal inflammatory exudates causes them to become viscid, ropy, and gelatinous. In simple inflammations, such as are seen in coryza, the exudate may consist of water and mucus, being colorless, transparent, and but slightly viscid. In other cases the admixture of pus causes the secretion to become thick, tenacious, and yellowish from the presence of the pus corpuscles.

The mucous metamorphosis of the connective tissues causes differing appearances according to its extent and mode of occurrence. If limited in extent and widespread, it may cause the whole tissue to appear slightly swollen and soft. If more marked, the moisture and softness are more pronounced and the tissue becomes lacerable and can easily be punctured by the fingers. If the process be still more localized and advanced, colliquation cysts form in the tissue—especially in morbid growths—and contain a ropy, tenacious, transparent fluid similar to that seen on the surface of the mucous membranes. Such fluid sometimes oozes out of the tumor when incised, or can be expressed from it.

Morbid Physiology.—The nature of the process is obscure. Mucus is an albuminoid containing C, O, N, and S. Three closely related bodies are formed in this degeneration—*i. e.*, mucin, pseudomucin, and paramucin. *Mucin* readily swells and slowly dissolves in water so as to form a tenacious, stringy, slimy, transparent, mucilaginous mixture. It is precipitated by alcohol and does not dissolve upon the subsequent addition of an excess of acetic acid. It is not precipitated by boiling or by tannin. When precipitated, it dissolves again in neutral salt solution and in dilute caustic potash and carbonate solutions. In the alkaline solutions it is gradually transformed into alkali-albuminate.

Pseudomucin also dissolves in water with the production of a similar slimy, ropy jelly. It is precipitated in threads by alcohol, the threads being again soluble in water. Acetic acid does not dissolve it. When boiled in diluted mineral acids it, like mucin, splits off a carbohydrate which in alkaline solution reduces sulphate of copper. Pseudomucin is most common in ovarian tumors and gives the contents a gelatinous consistence. The substance in these cases is probably formed by the epithelial cells.

Paramucin has been described by Mitjnkoff in the interior of an ovarian cyst. It differs from the pseudomucin in that it reduces sulphate of copper in alkaline solutions without previous prolonged heating with mineral acid.

Charcot-Leyden crystals often abound in the mucus of bronchial and other catarrhs, and may have some definite relationship to mucin.

Pathologic Histology.—1. The epithelial cells of mucous membranes show large vacuoles of the mucus in the distal part of the cell, giving the appearance known as "goblet cells." The cells in the walls of cysts may show the same appearance, but those in epithelial tumors usually show the cytoplasm to be filled with smaller rounded droplets or vacuoles. The nuclei of the cells seem to retain their integrity for some time, but ultimately they disappear and the cell becomes transformed into mucus.

2. The mucous degeneration of the connective tissues at first glance resembles edema, in that the component elements of the tissue are separated by some fluid substance. In addition to this, however, the components are much altered in distinctness from swelling and metamorphosis of the fibers and cells, so that the structure lacks the usual definiteness. The cells first show the presence of mucous droplets in the cytoplasm, next show destructive changes in the nuclei, which stain palely and often uniformly. Ultimately the entire substance of the cell is destroyed and disintegrates. The cells which longest preserve their integrity seem to be the fixed connective-tissue cells, and in tissues advanced in the degeneration spider and stellate cells of this type appear numerous. Mucin is precipitated by alcohol, so that the degenerated tissue, when hardened and treated in the usual way for microscopic study, shows a finely granular condition of the ground substance. The mucin granules are hematoxyloniphilic.

Special Forms of Mucous Degeneration.—**Myxedema** (*q. v.*) is a chronic disorder of nutrition characterized by mucous deposits in the areolar tissue of the face, neck, and breast, and accompanied by physical and mental deterioration. Myxedema (*cachexia strumipriva*) seems to depend upon removal or disease of the thyroid gland and is a true cachexia. The affected areas of the skin are peculiarly white, dry, rough, and soft.

Cretinism (*q. v.*) is congenital myxedema with succeeding dwarfing and idiocy. It occurs in congenital disease of the thyroid gland.

COLLOID METAMORPHOSIS.

Colloid metamorphosis is the conversion of the cell substance into a glue-like jelly known as colloid. It occurs only in epithelial cells.

A colloid substance constitutes the normal secretion of the thyroid gland and pituitary body. Under pathologic conditions it may occur in either gland in excess, leading to the formation of cysts (*colloid goiter*). It occurs very frequently in cystic tumors of the parovarium. It is also found in the tubules of the kidney in chronic nephritis, and in the prostate, forming some of the free bodies.

Etiology.—The cause of the disease is not known.

Morbid Anatomy.—Colloid forms a jelly of varying consistence, which is sometimes so thin as to be quite fluid, at other times so viscid as to be like thick calves'-foot jelly. It is usually clear and amber colored, but may vary, and sometimes appears bluish. It occurs chiefly in masses of homogeneous consistence.

The jelly-like masses commonly fill cysts of varying size, with which morbid growths may be honeycombed. In colloid tumors of the stomach with peritoneal extension and metastasis there may be free masses of yellow jelly in the peritoneum.

Pathologic Histology.—The colloid substance is formed by the epithelial cells, in which it at first appears in the form of droplets, which in the thyroid gland seem to escape from the cells and unite to form masses in the alveoli of the gland. From these alveoli the colloid substance enters the lymphatic vessels of the gland, through which it is absorbed.

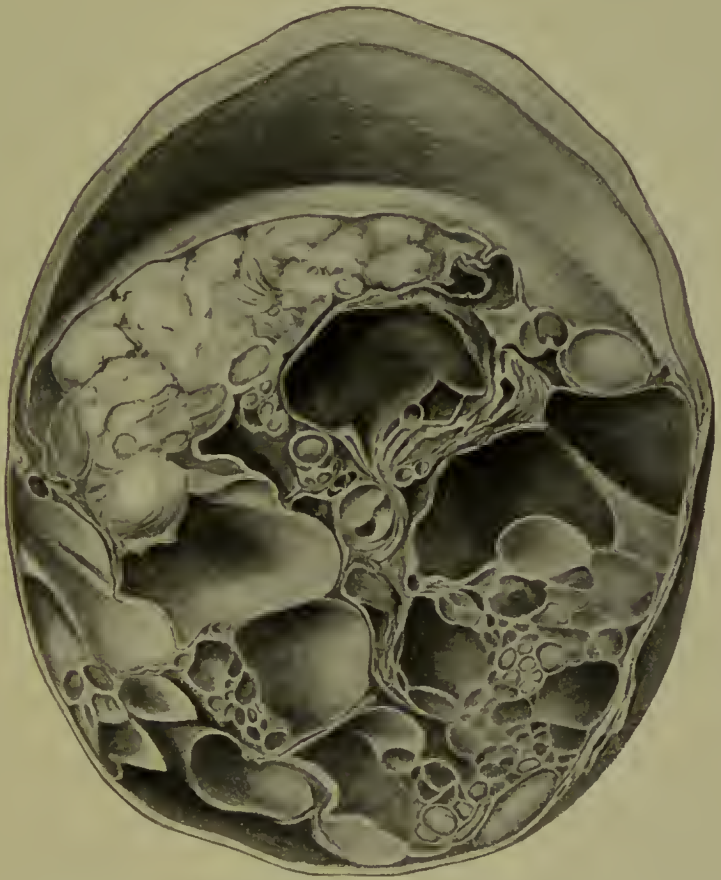

FIG. 70.—Cystoma of the ovary. The organ is divided by a longitudinal section, one half being shown in the illustration. Many of the cysts are distinctly shown, some of them being filled with colloid material.

The cells, however, both in the thyroid gland and in morbid growths, are commonly themselves completely destroyed and transformed into the colloid substance. It is by such cellular destruction that the cavities filled with colloid that occur in the morbid growths are formed. The intermediate stages of cellular destruction are not known.

Pathologic Physiology.—Colloid is an albuminoid whose nature has not yet been accurately determined. It varies in microchemistry at different times, and at present the term colloid is applied to what will in the future prove to be a number of different compounds. Colloid and mucoid degenerations are probably closely related to each other, but while the mucus swells in water, colloid does not; while mucus is precipitated by alcohol and acetic acid, colloid is not. It also colors orange by Van Giesen's stain.

In the kidney, especially in chronic interstitial nephritis, colloid substance is deposited in the tubules in the form of small, laminated, concentric spheres and cylinders. They are recognizable by their yellowish color and lack of affinity for nuclear stains.

Ziegler regards the prostatic concretions which fail to respond to the iodin tests as colloid in nature.

KERATOSIS.

Keratosis or hyperkeratosis is excessive cornification of epithelial cells.

Etiology.—It is observed in ichthyosis; lichen pilaris; keratosis follicularis or Darier's disease; keratosis obturans, a disease of the external auditory meatus with desquamation of superabundant epithelial cells, usually mixed with cerumen and cholesterin crystals; pityriasis pilaris, characterized by pin-head-sized conical elevations surrounding the hair follicles and partly resembling "goose flesh" and ichthyosis, the skin becoming dry, harsh, and like a grater; keratosis senilis, in which, upon the skin of the face and hands of old people, light or dark yellowish or brownish dry points with scaly character appear, which may form the starting-point of epitheliomata. It is also seen in certain slight inflammatory affections, such as scars, corns, etc.

Keratosis is also observed in tumors containing squamous epithelium, such as squamous epithelioma, hard papilloma, and cholesteatoma.

In the various skin lesions with which it is associated keratosis always occasions increase in the hard, dense, horny substance (callosities, corns, etc.).

Morbid Anatomy.—Extreme cornification is observed in the development of horns—*cornu cutaneum*—upon squamous epithelial tissues. They are most frequent upon the head and face, but have been observed upon the hands and penis and other parts of the body.

Pathologic Histology.—In abnormal conditions the deposits of eleidin or keratohyalin may occur in larger drops than normal and attract attention. It is such drops or masses that have been mistaken for intracellular parasites in many cases. The occurrence of the granules and loss of nuclear staining are quite characteristic.

In papilloma and epithelioma the keratin masses occur in the cell nests and interpapillary crypts, their size varying. They are often of a yellowish color, and always show more or less definite concentric arrangement of the component epithelial cells. It seems as if the formation of these bodies, which are known as "*epithelial pearls*," depended upon the abnormal environment of the cells, which, were they situated upon the surface, would desquamate, but being held in the crypts, are unable so to do.

Pathologic Physiology.—The epidermal cells all over the body develop from soft protoplasmic cells of the rete mucosum. As these cells, by the increase of subjacent cells, are gradually forced outward, they reach a point at which their cytoplasm becomes occupied by small granules (stratum granulosum). These granules consist of a substance known as *eleidin* or *keratohyalin*, which is to be used in cornification, and which seem to develop at the expense of the nucleus, for about the time the granules make their appearance in the cytoplasm of the cell its nucleus is found to have lost its chromatin and ceases to stain.

The keratohyalin in some manner pervades the cytoplasm, which becomes converted into a dense, hard, horny substance in consequence. By some this substance is supposed to be a form of colloid.

The nature of the process is no further understood than that it is an exaggeration of a normal function of the cells.

ATROPHY.

Atrophy is wasting of the tissues, and is characterized by diminished size and loss of functional activity. Atrophy may be general to the entire body or may affect parts only.

I. **General atrophy** or **emaciation** is a condition in which the entire body suffers wasting. It is best illustrated in starvation (*q. v.*), in the end-stages of which atrophy may reduce the individual almost to a skeleton. This form of atrophy occurs in starvation, wasting diseases, and diseases of the nervous system with errors of metabolism and trophic influence. It is remarkable to find to what a state of emaciation individuals may be reduced without obvious cause. Exaggerated cases of this condition are occasionally exhibited in museums as "living skeletons." Among the most interesting cases collected by Gould and Pyle is "Hopkin Hopkins, a little Welshman, who in 1754 died of old age and gradual decay, aged seventeen years, and who had been exhibited in London as a natural curiosity; he had never weighed over 17 pounds, and for the last three years of his life never more than 12 pounds." Among the cases of emaciation following extreme muscular atrophy was Rosa Lee Plemons, who at the age of eighteen years weighed only 27 pounds. The emaciated persons are usually sickly and lacking in vital resisting power.

II. **Local Atrophy.**—Atrophy of parts of the body may be *simple*—that is, depend upon reduction in the size of the component elements, or *degenerative*, depending upon destruction of some of the elements of the part. Degenerative atrophy is the usual form.

Atrophy may also be *active* or *passive*. *Active atrophy* depends upon the inability of the cells properly to appropriate the nourishment brought to them; *passive atrophy* is caused by insufficient nourishment reaching the cells.

Etiology.—Atrophy may be physiologic or pathologic.

(*a*) *Physiologic atrophy* depends upon inactivity. The muscles when exercised enlarge or hypertrophy, as in the athlete; when no longer exercised, their volume is only a source of expense to the economy, and they are accordingly permitted to waste, their substance being otherwise utilized.

In the development of the lower animals, and to a less extent in man, certain organs useful during certain periods of life disappear at other periods. Thus, the tail of the tadpole, while very useful to the aquatic embryo, is useless and incommodious to the amphibious frog, and accordingly rapidly atrophies about the time the gills disappear and the lungs expand. Both tail and gills undergo simultaneous atrophy. In the embryo certain structures, without which its development could not progress, undergo subsequent atrophy and may entirely disappear. Among those of the human embryo we may mention the urachus, which connected the bladder with the umbilicus; the round ligament of the liver, the omphalomesenteric duct, the hypogastric arteries, etc. Organs which were of use to antecedent animals, but which have not yet become extinguished in the evolution of species, sometimes persist in existing species, growing to unnecessary proportions in the early development, but atrophying later. This is well illustrated in the case of the thymus gland, which is an important organ in gill-breathing animals, but apparently useless in mammals. It grows rapidly in the embryo, is large in the child at birth, but after birth atrophies and frequently entirely disappears with the attainment of adult size.

Organs which cease to be useful because of the age of the individual also atrophy; thus, after the menopause the uterus and ovaries, having no further function to perform, begin to atrophy, and in the course of years become quite small and relatively fibroid.

(*b*) *Pathologic atrophy* may with difficulty be separated from physiologic forms. Its chief causes are:

1. *Senility.*—In old age organs which have outlived their function, as, for example, the sexual organs of women, undergo physiologic atrophy. Pathologic atrophy in old age may be secondary to vascular changes, as in the local loss of substance shown by the pits and furrows on the surface of the senile kidney, the thin, shining, somewhat scaly skins of the aged, the disappearance of the hair follicles, the alteration in the bones following loss of the teeth, and the preponderance of compact over spongy tissue in the bones, depending upon the disappearance of the metabolic elements of the osseous tissues.

2. *Pressure.*—Pressure is a common cause of atrophy. The foot of the Chinese lady, which was kept bandaged in babyhood, suffers both hypoplasia and atrophy in consequence of the pressure. The tight corsets formerly fashionable among our own women, by turning in the costal margins, cause them to press upon a depressed liver, where the pressure causes a marked loss of substance, so that the liver may actually be divided into two parts, connected only by fibrous tissue ("Schnurleber").

The pressure of the thongs of heavy leather aprons worn by smiths and others may cause atrophy of the subcutaneous tissues pressed upon and lead to the formation of a constriction corresponding to the position of the thong. The pressure of a truss worn to keep back a hernia produces atrophy of the tissues pressed upon. The pressure of morbid growths in any part of the body may lead to atrophy of the contiguous organs. The cicatricial tissue formed in the organs in certain chronic inflammatory diseases, such as cirrhosis of the liver, contracted kidney, etc., causes atrophy of the parenchyma by pressing upon it.

3. *Malnutrition.*—Ischemia is a common cause of atrophy. If the blood supply be entirely interrupted, the part undergoes necrosis, but if it be partially interrupted, it undergoes atrophy. This is well shown by the atrophic disturbances following arteriosclerotic changes in old age, and in atrophic changes succeeding thrombosis and the pressure of morbid growths upon vessels.

4. *Inactivity.*—Pathologic conditions of the motor nervous apparatus, such as are seen in hemiplegia, paraplegia, monoplegia, in which only the motor apparatus is interrupted, are succeeded by atrophy of inactivity without any failure of normal influence. Atrophy from inactivity is also well illustrated in the remaining muscles of amputated limbs.

5. *Failure of trophic innervation* is one of the most frequent and most pronounced causes of atrophy. Thus, in peripheral neuritis, poliomyelitis, and the muscular dystrophies the failure of trophic innervation is succeeded by atrophy.

Morbid Anatomy.—The atrophy of the whole body is, of course, symmetric. Atrophy following symmetric nervous lesions may also be symmetric, but the greater number of atrophies are asymmetric.

The atrophied part is smaller than normal, though otherwise resembling the normal part. When certain muscles of the limbs atrophy while their opponents are preserved, the limb may become deformed by the activity of the healthy muscles, and many cases of club-foot and club-hand can be thus explained.

When atrophy is irregular in distribution, as in arteriosclerosis of the kidney and cirrhosis of the liver, the surface of the organ may be marked by pits, fissures, and other irregularities. If the atrophy be uniform, it is smooth.

Pathologic Histology.—In simple atrophy the component elements of the part may be visibly smaller than normal. This can be well observed in the muscular tissues, in which many minute fibers are present among normal-sized fibers.

Degenerative atrophy has accompanying whatever loss in size the elements may suffer, the additional picture of fatty metamorphosis or whatever other necrobiotic process may be present.

In the so-called brown atrophy of the heart the muscle cells contain granules of pigment clustered about the ends of the nuclei.

Morbid Physiology.—Together with the reduction in the volume of the affected part, the physiologic activity is also necessarily reduced.

In paired organs, such as the kidneys, compensatory hypertrophy of the other organ usually occurs and increases the apparent disproportion in size, though continuing the function. The atrophy of any part is accompanied by a corresponding reduction in the size of its nutrient vessels.

NECROSIS.

Necrosis is death of a part of the living organism. It is local death as differentiated from somatic death, or death of the entire organism. The dead part may be an external extremity, or may be an internal organ surrounded on all sides by still living and comparatively normal tissue.

Etiology.—The causes of necrosis may be summarized as follows:

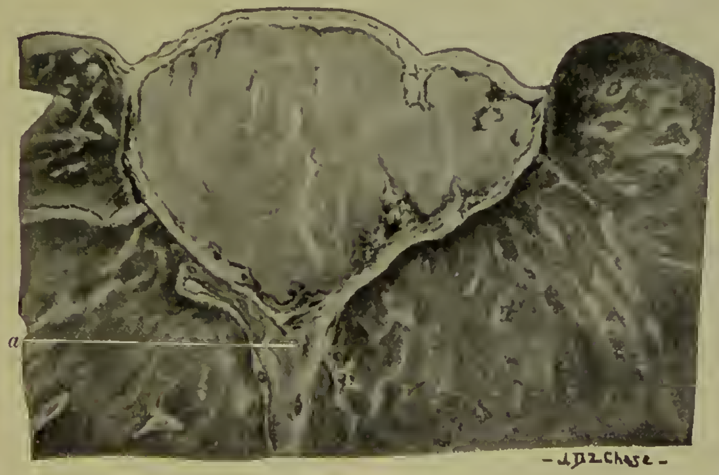

FIG. 71.—Anemic infarct of the spleen: *a*, Vessel with organized thrombus.

1. **Mechanical injury** may so disorganize and comminute a tissue that its component cells, unable longer to maintain their integrity independently of the integrity of the whole part, must die.

2. **Thermal injuries** are very destructive in tendency. Temperatures above 35° to 65° C. destroy the vitality of the cells in a comparatively short time, while higher temperatures, such as 100° C., do so immediately. Temperatures at the opposite extreme do an equal amount of injury, and freezing is a frequent cause of gangrene.

3. **Chemical injuries** not infrequently occasion necrosis and gangrene. Carbolic acid, the mineral acids and alkalies, all cause necrotic and gangrenous lesions of the parts touched.

4. **Infection** may cause necrosis and gangrene. This is in reality a form of toxic or chemical necrosis, as the bacteria act through their metabolic products. The diphtheria bacillus causes a superficial coagulation necrosis of the surfaces upon which it grows, and its separated toxic products when applied repeatedly to some delicate tissue, such as the conjunctiva, cause necrosis of the superficial cells.

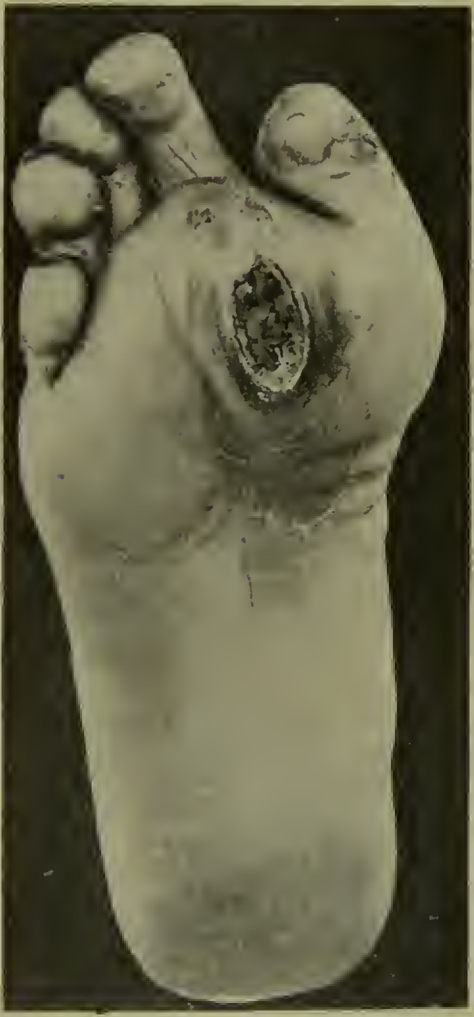
FIG. 72.—Perforating ulcer of the foot in a tabetic subject (Matas).

The irritating products of the tubercle bacillus—possibly the acid separated by de Schweinitz and others—are the cause of the cheesy necrosis of the tubercles. The micro-organisms of suppuration, partly through their own enzymic products, occasion the colliquation necrosis characteristic of suppuration. Infection by the diphtheria bacillus is found to cause gangrene of the cheek and genitalia in the disease known as *noma*.

5. **Malnutrition** is a very common cause of necrosis. If the nutrition is gradually withheld, necrobiosis with atrophy occurs, but if the nutrition is completely shut off, necrosis must occur. Such changes are sometimes found after the ligation of arteries, and sometimes after ligation of the great veins, where on the one hand the collateral circulation is inadequate to supply the needs of the part, or on the other hand the retention of venous blood in the part interferes with its oxygenation and nutrition. Similar necrosis is seen to succeed thrombosis and embolism. Pressure of neoplasms and other morbid growths may cause necrosis by gradually interrupting the blood supply until after primary necrobiosis; secondary necrosis occurs after the diminution of the blood supply becomes extreme.

Arteriosclerosis with gradual destruction of the vessels is a common cause of that form of necrosis known as senile gangrene.

6. **Trophic disturbances** predispose to necrosis by diminishing the resisting powers of the tissues. Thus, in many forms of spinal disease the tissues readily succumb to the trauma occasioned by the pressure of the bed upon which the patient lies, and necrosis occurs at the points pressed upon. This form of necrosis is commonly spoken of as a *decubitus* or "*bedsore*." Other examples of this form of necrosis are the keratitis following injury of the fifth nerve, and the *perforating ulcer* of the foot. A peculiar necrotic affection of the little toe occasionally seen among the dark-skinned races of

the tropics is known as *ainhum*. Its true cause is not determined; it may be trophic or may depend upon local cicatricial tissue formations.

7. **Cachexia** and other conditions of depraved vitality predispose to necrosis and gangrene by affording an unusual opportunity for the invasion of the tissues by bacteria and by reducing the vitality of the tissues. Thus, in typhoid fever bedsores are frequent, and in diabetes mellitus local gangrene of the skin is common. In feeble infants and badly nourished children *noma* of the cheek and vulva occasionally makes its appearance.

Varieties.—Necrosis is usually evident both to the naked eye and to the microscope because of the retrogressive changes taking place in the tissues.

1. **Coagulation Necrosis.**—This is death with consolidation or condensation of the tissue. The process is variable and not fully understood. It is best illustrated in the coagulation of the blood, where the union of fibrin factors and ferment, through the formation of a new substance (fibrin), transforms the fluid blood into a solid mass. Coagulation necrosis of the same kind is seen in some cases of interstitial hemorrhage and in numerous forms of the inflammatory exudates, especially those of croupous pneumonia and diphtheria, in both of which true fibrin is formed.

Fibrin is, however, not formed in other varieties of coagulation necrosis, though it is not improbable that some related body may be formed through the action of ferments derived from the cells upon the lymph and juices. It is possible in this manner that the coagulation necrosis of the spleen and kidney succeeds anemic infarcts.

In other cases, as in the form known as *caseation* (*cheesy necrosis* or *tyromatosis*), in which a cheese-like mass is formed through the action of bacteria upon the cells, it is possible that the bacteria furnish the essential ferment. Caseation is seen in its most typical form in the tubercle, where the cheesy matter has a consistence varying from that of cream cheese to that of the more solid forms, and may be firm or crumbly.

2. **Colliquation Necrosis.**—This is death followed by liquefaction of the tissue. It is best illustrated by the anemic infarctions of the brain that follow embolism. The nervous substance first degenerates (fatty and hyaline degeneration), then melts away into a semi-fluid mass, from which the necrotic matter is slowly absorbed, while the fluid itself remains to form a cyst (colliquation cyst).

Colliquation necrosis is also illustrated by suppuration, where even solid and resisting structures, such as tendons, cartilages, and even bone, melt away before the bacteria and pus cells.

3. **Mummification (Dry Gangrene).**—This is death followed by inspissation of the tissue. It can occur only when the dead tissue is superficial and can be acted upon by the air, and when the conditions under which the necrosis has developed have determined that the tissue contains but little moisture. The stump of the umbilical cord undergoes dry gangrene or mummification.

Mummification is most frequent in senile disease of the arteries with obstruction of the circulation of the extremities of the body. The toes are the usual seat of the disease.

Frost-bite, if the tissue freeze at a time when it is bloodless, may also cause mummification. Ergot-poisoning with permanent spasm of the arteries may also cause it. Certain paroxysmal contractions of the vasoconstrictors, as occur in Raynaud's disease, may also lead to dry gangrene.

4. **Gangrene** is necrosis accompanied by putrefaction of the tissue. It occurs almost exclusively in parts of the body subject to external infection. Thus, it may succeed any form of necrosis and many simple lesions of the

extremities followed by infection. Putrefaction cannot take place in living tissues; hence, for the occurrence of gangrene it is essential that necrosis first occur. The necrosis may depend upon any of the causes already given or upon an extremely violent infection of any nature sufficient to devitalize the tissue. The *hospital gangrene* which was the dread of the surgeon before the days of Listerism, and which caused great numbers of deaths, in military hospitals especially, was only a violent infection of the wound, succeeded by necrosis and putrefaction of the tissues.

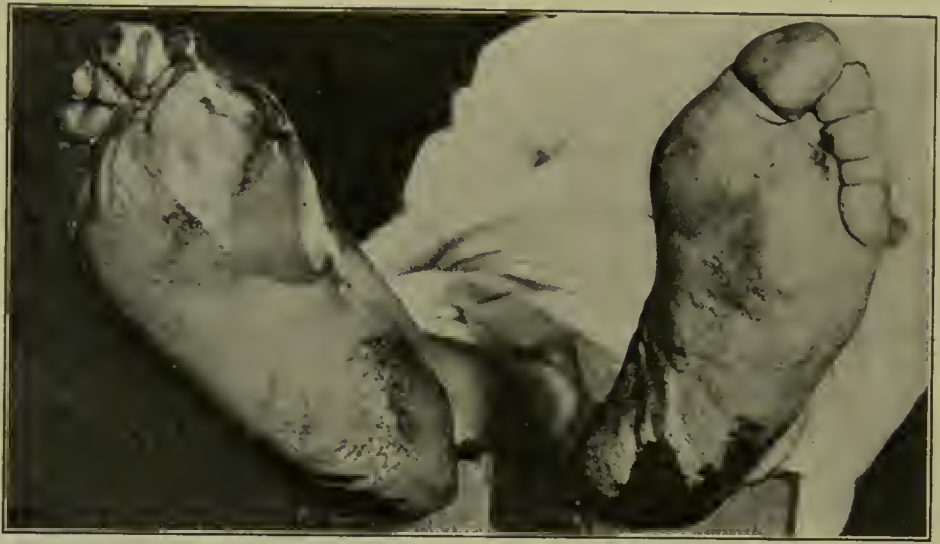

FIG. 73.—Symmetric gangrene of the feet.

Gangrene most frequently affects extremities of the body. It may affect local areas of the skin in *gangrene diabeticorum*, these areas being of irregular distribution.

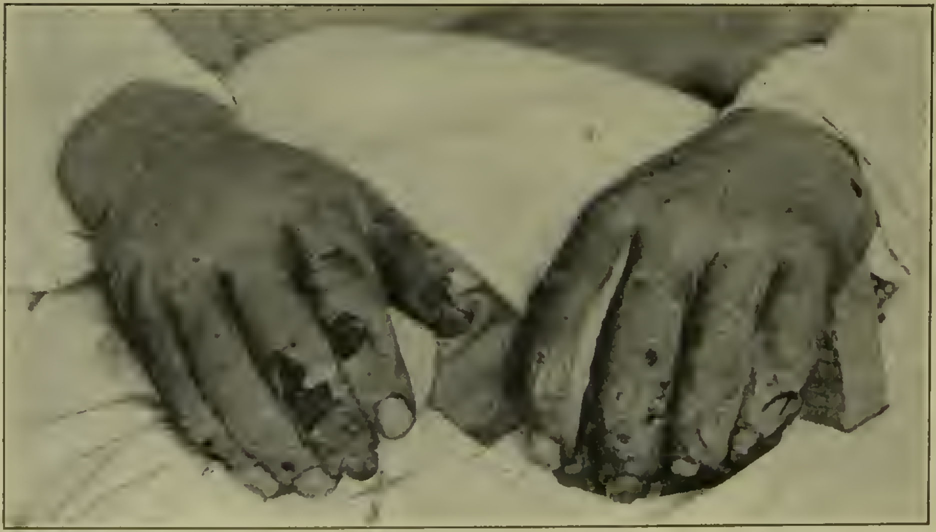

FIG. 74.—Symmetric moist gangrene of the hands. The cause of the gangrene was never determined (from a case in the Medico-Chirurgical Hospital of Philadelphia).

Noma is a gangrenous affection of the cheek, seen in impoverished children. It commences in the interior of the cheek and soon invades its entire thickness, appearing upon the face. It may also occur upon the genitalia, which may be destroyed or deformed in consequence. The affection is commonly fatal, and leaves unsightly deformities if recovery takes place. According to recent researches, the disease is caused by the diphtheria bacillus.

Gangrene of the lung may depend upon infection of devitalized areas through the inspired air. It succeeds pneumonia, hemorrhage, etc., and may occur in a circumscribed or diffuse form.

Gangrene of the intestine may occur in strangulated hernia and in volvulus and intussusception, the necrotic conditions brought about by the interrupted circulation being succeeded by infection from the intestinal canal.

The occurrence of decomposition in the gangrenous lesions naturally gives them an offensiveness not possessed by any of the other necrotic lesions. It also leads to the formation of gas blebs in the tissues, which are not found in other lesions, and to the transformation of the tissue into a dark-colored, slimy, pulpy, stinking mass.

Morbid Anatomy.—The naked-eye appearance of necrotic tissue varies with the form, extent, and condition of the tissue affected. Gangrenous parts are for the most part greenish black in color, slimy, and lacerable in texture. Mummified parts usually appear black and dry. Necrotic areas following infarctions of the kidneys and spleen are grayish or yellowish and soft. Necrotic changes in the nervous tissue, according to the presence or absence of blood, etc., may present themselves as *red softening*, *yellow softening*, or *white softening* (*q. v.*).

Colliquation necrosis is characterized by the melting away of the tissues; coagulation necrosis by firmer, sometimes crumbly or cheesy, collections.

Pathologic Histology.—Necrosis differs from necrobiosis in that the changes are more rapidly destructive and more widespread. The actual changes by which necrosis occurs consist in part of the same changes that are observed in the metamorphoses. Thus, fatty changes are common in the necrotic tissues, and mucous metamorphosis leads to a slimy formation not unlike the slimy matter occurring in gangrene.

Microscopic examination of the necrotic tissue shows that the cells are more homogeneous than normal, and that the nuclei lack ability to retain the stain. The nuclear substance seems to break up and disseminate itself throughout the cell in the form of irregular, tingeable fragments. Later these fragments disappear and all traces of cellular structure are lost. The intercellular substance shows changes in an order corresponding to the density and resisting power. The fibers of the connective tissue swell and become indistinct preparatory to solution. Cartilage and ligaments slowly melt away, bone resists almost indefinitely, and when spontaneous recovery takes place in gangrenous limbs, the bones often remain protruding from the end of the stump.

In coagulation necrosis, if fibrin be formed, it appears as homogeneous masses between the tissue elements or as threads forming a reticulum between the cells. In cheesy necrosis the caseation is characterized by the formation of hyaline and fatty granules. In the preliminary steps of this caseation the cells become hyaline and show a pronounced disposition to cohere and later to unite, with the formation of protoplasmic masses (giant cells). Later these giant calls, like the other cells of the tissue, break up into indefinite granules. Such cheesy areas take no stain, and usually show a slightly yellowish color in microscopic sections.

In necrotic tissue it not infrequently happens that the retrogressive changes lead to the formation of new chemical compounds, which may appear in the tissues. Of these, cholesterin, leucin, tyrosin, and crystals of the fatty acids are most frequent and easily recognized. Gangrenous tissue is also found to be replete with saprophytic bacteria.

A zone of inflammatory reaction always surrounds an area of necrosis, or occurs between it and the nearest healthy tissue.

Terminations.—1. **Exfoliation of the Sphacelus.**—This occurs in gangrene and other forms of superficial necrosis. The dead tissue is known as the *sphacelus* or *slough*. The effort of the organism is to separate the dead from the living tissue. The dead tissue, probably in consequence of the changes to which it is subject and the new chemical compounds that are formed within it, is a source of continued irritation and injury to the sound tissue against which it impinges. The result is that at this point of contact a zone of inflammation occurs—the *line of demarcation*. In gangrene of the limbs the formation of this line of demarcation is looked for with the greatest interest by the surgeon, as indicating that the gangrene has reached its upper limits, and as soon as the line forms entirely around the limb, amputation can safely be performed above it.

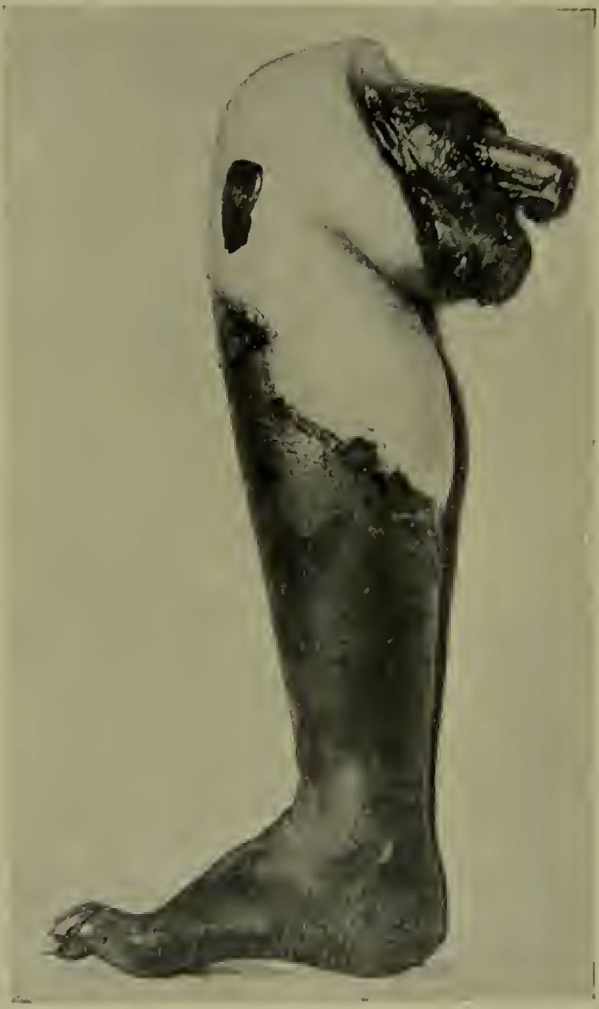

FIG. 75.—Senile dry gangrene of the lower extremity, showing line of demarcation (Hektoen).

If such a line of demarcation be carefully examined, it will be found that the dead tissue is actually separated from the living tissue, and that between them an interval is forming and widening. As the dead tissue separates from the living tissue, an ulcerated surface of living tissue is exposed. This was known to the surgeons as the *line of ulceration.* It soon becomes covered with granulations, and the process of active repair goes on hand in hand with the separation of the sphacelus. The presence of bone in the gangrenous extremities complicates the process of repair and makes it practically impossible for nature to secure a satisfactory result, as after the complete exfoliation of the mass the bones remain protruding. Surgical interference is, therefore, necessary for the successful management of the stump.

When the gangrene or necrosis involves simply the soft tissues, as in diabetic gangrene of the skin and in noma, the exfoliation of the sphacelus is much more simple and can be permitted to take care of itself.

2. **Sequestration and Encapsulation.**—These occur when the necrotic tissue is for any reason prevented from being exfoliated.

Sequestration is seen in necrosis of the bones following injury or infection. The necrosis is followed by separation of the periosteum, but before the dead lamella of the bone can be exfoliated, an ossifying periostitis (*q. v.*) occurs with the formation of new healthy bone about and partly upon the dead lamella. The dead tissue is thus caught or sequestered, and is in consequence called a *sequestrum.* Its presence and slow retrogressive changes prevent perfect recovery, and in cases of bony necrosis with the presence of a sequestrum open sinuses communicating with the exterior remain until, after months or sometimes years, the sequestrum is eliminated, after which the wound heals. As the presence of the sequestrum is the cause of all the trouble, its surgical removal is followed by immediate recovery.

Encapsulation of the necrotic tissue occurs in the deeper organs, where its position makes it impossible for the dead tissue to exfoliate. The dead tissue having completed its retrogressive changes is little by little absorbed, the contracting scar tissue following it as it diminishes in volume, until, at length, only a fibrous node remains. Such changes are seen in infarcts of the spleen and kidney. If the encapsulating connective tissue does not contract, the absorption of the necrotic tissue leaves a cavity filled with clear fluid (colliquation cyst), as in infarcts of the brain.

3. **Absorption.**—Absorption of the necrotic tissue usually follows necrosis of the internal organs, such as is observed after vascular disturbances—thrombosis, embolism, infarction, etc. It may be preceded by the reactive inflammation above described. The absorption of the necrotic tissue may be complete, no traces of the original structure remaining.

Absorption follows colliquation necrosis more readily than it does coagulation necrosis.

4. **Calcification.**—When the solution and absorption of necrotic tissue are delayed, lime salts are apt to be deposited in the mass. It thus happens that old tubercles with cheesy necrosis calcify; that *phleboliths,* or vein stones and *arterioliths,* or artery stones, are formed in consequence of thrombosis, and that lime salts are found in the cicatrices of old infarcts, abscesses, gummata, etc.

5. **Cicatrization or Organization.**—In this mode of termination the necrotic tissue forms a framework in which connective-tissue formation occurs. It is best illustrated in *thrombo-arteritis* and *thrombophlebitis* (*q. v.*) which succeed thrombosis and terminate in organization.

DEATH.

Death is the cessation of life. The term applies to the organism as a whole, all its component elements ceasing to live.

Death is the natural termination of life, all known living beings being mortal. Although the reintegration of the tissues by the intussusception of new matter is one of the phenomena characteristic of life, there comes a time when this intussusception of new matter fails and the cells die, the death of certain groups of cells determining that the whole organism must die.

Death may be *physiologic* or *pathologic*. The former occurs after a length of life recognized as that normal to the species, from general wearing out of the cells of the body and their inability longer to carry on its functions. Pathologic death occurs from unnatural causes, at a time when the individual is not yet worn out and when the cells are still active. When a careful analysis of the two conditions is made, however, it is not possible in all cases to separate physiologic from pathologic death.

A brief reflection will soon convince one that all parts and functions of the body are not essential to life. The motor apparatus, through amputation of the limbs or general paralysis, may be entirely put out of service, yet life continue unimpaired. The sexual organs have nothing whatever to do with the maintenance of life. All the special sense organs may be destroyed, yet life continue just the same. Thus, one by one eliminating the functions, all of which are essential to health, we find that only three are indispensable to life—*circulation*, *respiration*, and *innervation*.

Life is impossible in a differentiated organism unless a nutritious fluid is circulated among its cells, and unless this fluid be properly aërated; and the maintenance of this circulation is impossible without a regulating nervous mechanism; hence, life rests upon this tripod, and when any one of the essential functions is suspended, must almost immediately cease.

The term death, as we have thus far employed it, signifies *somatic death*, or death of the individual. It is succeeded some time later by *molecular* or *cellular death*. In somatic death all those phenomena which we recognize as making up life cease, but the cells live on and many of their activities can be observed for hours afterward. This persistence of cellular life after somatic death is far better illustrated by experiments upon the cold-blooded animals than upon man. The tail of the snake continues to move "until the sun goes down." The head of a decapitated tortoise can still hold a stick in its jaws, and its heart suspended in salt solution continues to pulsate for many hours. The decapitated rattlesnake will "strike" exactly like the normal reptile and continue furiously to shake its rattles. These movements, which may continue for hours, are an exaggeration of the muscular twitchings that one often sees in the freshly quartered cattle in slaughter-houses.

That certain of our cells long retain their vitality after the occurrence of somatic death seems to be shown by what appear to be authentic cases of considerable growth of the hair and nails after death.

Signs of Death.—In addition to the cessation of circulation and respiration, upon which dependence is commonly placed to determine whether or not life has become extinct, the following *infallible signs of death* are of importance:

1. *Algor mortis*, or the coldness of death. With the cessation of life metabolism ceases and the temperature falls to that of the surrounding atmosphere. The fall of temperature may occur in an hour or two, or may be delayed twelve or even twenty-four hours. In hot weather, of course, this sign becomes unimportant. In some cases, such as death from tetanus, the temperature may continue to rise for a few hours after death.

2. *Rigor mortis*, or *cadaveric rigidity*. The stiffness of death depends upon the coagulation of the contractile substance of the muscles. It comes on in from four to twelve hours in ordinary cases, but may occur almost immediately when death has been sudden. It is said that upon battlefields, where men and horses have been instantly killed by bullets, they are found standing or half reclining in almost the identical position assumed at the moment of death. In very slow death from cachexia and marasmus rigor mortis may not appear for twenty-four hours. It begins in the muscles of the jaw and neck, is most marked at the knees and hips, and seems to continue longest in the hands and feet. When once established, it continues until decomposition comes on.

3. *Livores mortis*, or the spots of death. *Cadaveric lividity* consists of a livid, purplish discoloration of the dependent parts of the dead body, caused by the gravitation of blood from the capillaries of the upper to those of the lower part of the body. The color varies according to the oxygenation of the blood. If the superficial vessels were full before death and the patient cyanosed, the spots will be dark. In CO-poisoning they are said to be red. The parts of the body that touch the table remain pale, because of the inability of the blood to enter the compressed capillaries. Pressure upon one of the spots is followed by pallor, caused by the expression of blood from the capillaries pressed upon into other vessels. Cadaveric lividity appears in from six to twelve hours and remains. The upper part of the dead body is very pale and white for the same reason that the dependent part is livid—that is, because of the gravitation of the blood.

4. *Putrefaction*. Putrefaction is an infallible sign of death; its appearance varies in time with the temperature and the condition of the body at the time of death. In hot weather putrefaction progresses much more rapidly than in cold weather. Badly infected bodies, as those in which gangrene or septic processes have occurred before death, putrefy more quickly than do others. It is said that the bodies of those dying from venom-poisoning putrefy more rapidly than do others.

5. *Loss of tissue elasticity*. A dead body flattens where pressed upon by the table or bed, and upon being raised does not assume its normal rotundity. The low temperature, by congealing the fat of the subcutaneous tissue, and the occurrence of rigor mortis in the compressed muscles explain the loss of elasticity.

6. *Relaxation of the sphincter muscles*. The eyes of dead persons usually open, the mouth opens and the jaw drops, feces are passed as the sphincter ani relaxes, and the urine dribbles.

7. *Loss of transparency of the cornea and dilatation of the pupils*. The pupils dilate at the moment of death; the cornea shortly becomes clouded. The eyes usually look directly forward and are expressionless.

CHAPTER VII.

PROGRESSIVE TISSUE CHANGES.

HYPERTROPHY.

In the broad sense in which it is frequently employed, hypertrophy is, as its etymology indicates, any kind of an overgrowth of the body. It is, however, customary to speak of true and of false hypertrophy, and to apply the term *hypertrophy* to the former, and *hyperplasia* to the latter.

I. *Hypertrophy* or *true hypertrophy* is a uniform enlargement of a part, depending upon increase in all its component elements. Such an enlargement is almost necessarily accompanied by an increase of functional capacity, and, in fact, most hypertrophies are physiologic in origin and significance. They may be either congenital or acquired.

Etiology.—Hypertrophy may depend upon:

1. **Congenital Impulse.**—Certain rare cases of enormous overgrowth of certain members during prenatal and postnatal life can at present be accounted for only by reference to some impulse experienced during development. Cases of giant growth of the fingers and toes are included in this class. Some defect in the organogenetic influences of the body must be at the bottom of these overgrowths, but the mechanism of their formation is not understood.

2. **Exercise.**—Unusual exercise demands increased energy. When, therefore, any part of the body is unduly active, Nature undertakes to compensate for the tax placed upon it by increasing its substance by a true hypertrophy of all its parts, so that its function may be increased to supply the demands made upon it. Such growth is, therefore, known as *compensatory* or *physiologic hypertrophy*. Familiar examples are the well-developed muscles of the athlete, the arm of the blacksmith, the heart obstructed by valvular defects, and the kidney when its fellow is diseased, hypoplastic, or removed.

3. **Nervous Impulses.**—These act in response to stimuli and appear to be reflex in character. Shortly after conception takes place the mammary glands become sensitive and enlarge to meet the expected demands of lactation. When a large part of the thyroid gland is removed, the hypophysis cerebri undergoes hypertrophy in consequence.

4. **Disease of the hypophysis cerebri** is associated with *acromegaly* (*q. v.*), a disease characterized by hypertrophy of the tissues of the face and extremities.

Hypertrophy is said to be simple or numeric. In *simple hypertrophy* the size of all the component elements of the part is increased. This condition is seen in the uterus during pregnancy. In *numeric hypertrophy* the number of the component elements is increased. This condition is more characteristic of hyperplasia than of hypertrophy. The truth probably is that in true hypertrophy both the size and number of the elements are increased.

Morbid Anatomy.—The hypertrophied part preserves its configuration, but is larger than normal. It shows no variations of color, consistence, structure, or function other than are compatible with its increased size.

Morbid Histology.—Except when the cells are measured to show that they are larger than normal, the hypertrophic part shows no histologic departure from the normal. During the growth of the hypertrophic part an increased number of dividing cells may be present, so that the tissue may more closely resemble that of youth than that of adult life.

Special Forms of Hypertrophy.—**Gigantism.**—Gigantism is hypertrophy or excessive growth of the entire body. The excessive growth may begin in intra-uterine life, so that when the child comes to term it is abnormally large. Gigantism is, however, usually dependent upon prolonged and rapid growth during adolescence. It depends upon exaggeration of the normal growth at the regular time and is impossible late in life. As will be shown below, attempted growth in later life fails to occasion any increase in stature because of the union of the shafts and epiphyses of the bones, and only provokes irregular enlargements of the extremities (acromegaly). The giant is rarely vigorous or powerful in proportion to his size, the vigor of growth apparently being accompanied by diminution of the general vital powers. Giants, therefore, are commonly of delicate and feeble physique. It is impossible accurately to define what shall constitute a giant. The average height of men in the United States is approximately 5 ft. 7 in., but

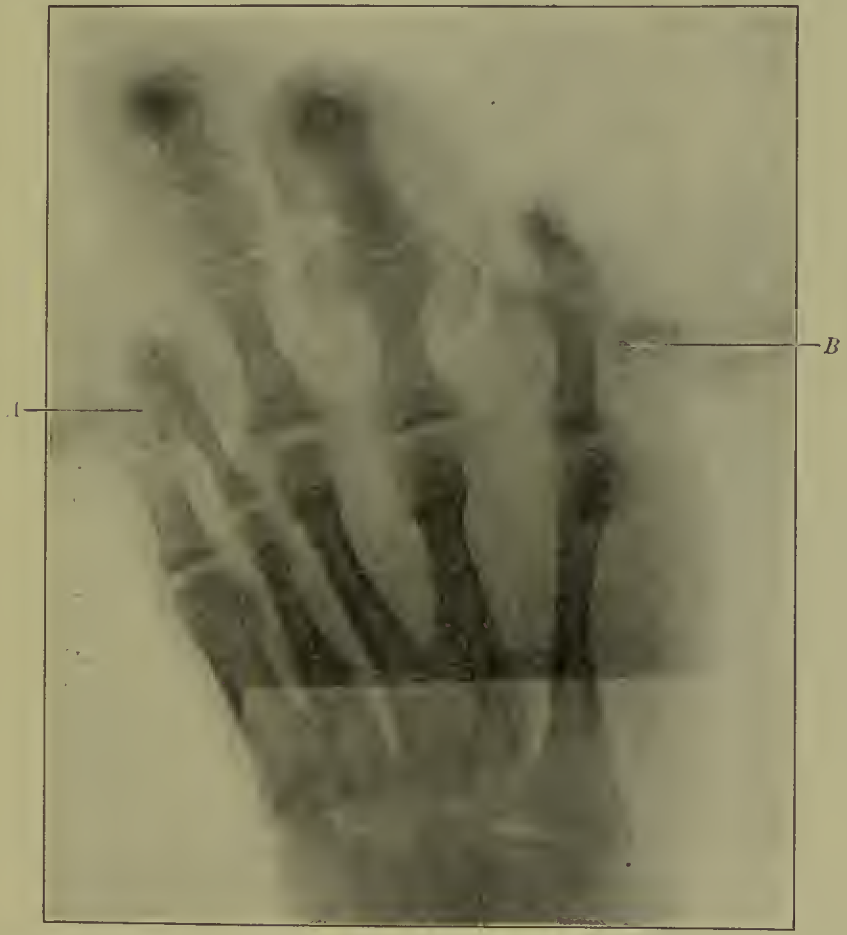

FIG. 76.—X-ray picture of the right foot of a boy with congenital hypertrophy of the third, fourth, and fifth toes, showing that the bones as well as the soft parts are involved in hypertrophy. *A* is the great and *B* the little (?) toe (from a case of Dr. James P. Mann).

every one knows men, not regarded as in any way unusual, who measure 6 ft. 1, 2, or 3 in. Exceptionally tall men measure 6 ft. 4 in.; unusually tall men of 6 ft. 6 or 7 in. occur, yet do not merit the term giants, so that there is no limit between tall men and giants any more than between short men and dwarfs.

Many of the giants have found it profitable to exhibit themselves, and have attained celebrity in this way. The measurements given under these circumstances are, however, rarely reliable. Of the well-authenticated giants, Gould and Pyle mention the "Irish Giant" (O'Brien), whose skeleton was in the collection of John Hunter. He was supposed to be 8 ft. 4 in. tall, the skeleton measuring 92¾ in. Patrick Cotter, another "Irish Giant," measured 8 ft. 4 in. at the time of his death. Captain Bates, familiarly known as the "Kentucky Giant," who was a familiar exhibitionist in this country from 1866 to 1880, measured 7 ft. 2½ in. and was well proportioned, weighing 450 pounds. His wife, Anna H. Swann, the "Nova Scotia Giantess," was 7 ft. 5½ in. in height.

The *etiology* of gigantism is obscure. Examinations of the skulls of giants have shown an abnormal size of the sella turcica, suggesting disease of the pituitary body.

Acromegaly, which will be again mentioned in connection with the diseases of nutrition and metabolism, is a second form of giant growth, characterized by true hypertrophy of the features, hands, and feet, occurring in adult life, and usually being associated with disease of the pituitary body. The relation of gigantism and acromegaly is probably very close. Gigantism is excessive growth during adolescence; acromegaly, excessive growth in adult life. Both conditions appear to be associated with enlargement or disease of the hypophysis cerebri. In some cases acromegaly seems to be hereditary.

The disease occurs in both sexes, though more frequently in men. It usually appears at or subsequent to middle life. It comes on insidiously, and there are a gradually increasing enlargement of the features and an overgrowth of the hands and feet. The face may change, so that the sufferer becomes almost unrecognizable to those who have not seen him for some time. The malar bones are greatly increased, the nose becomes wide and thick, the supra-orbital ridges become prominent, the jaw enlarges, and the expression becomes dull. The hands and feet may be enormous and out of all proportion to the size of the individual.

When a dissection is made and the tissues examined, a true hypertrophy is found, but the overgrowth is irregular in some particulars. Thus, the increase of bony substance is accompanied by the formation of numerous exostoses of small size and irregular form.

II. *False hypertrophy* or *hyperplasia* causes asymmetric enlargements, depending upon increase of the tissues. It is an exceedingly common morbid process, and may occur in almost any tissue and in any organ. The tissue most frequently hyperplastic is the fibrous connective tissue.

Etiology.—The causes of such hyperplasia as enters into the formation of tumors are obscure, but can be referred to:

1. **Irritation.**—The reaction of the tissues to a mild degree of irritation is usually accompanied by hyperplasia. Severe irritation provokes degeneration or inflammation. The irritations leading to hyperplasia may be:

(*a*) *Mechanical.*—The presence of a foreign body in a tissue is usually succeeded by a surrounding growth of connective tissue.

The wearing of a tight shoe, by inducing mechanical pressure upon the skin of the toes and provoking hyperemia, frequently occasions hyperplasia of the epithelial tissues, accompanied by keratosis and the formation of a corn.

The obstruction of the lymphatics by certain parasites, such as filaria, together with the local irritation the worms may cause, sometimes leads to enormous hyperplasia of the subcutaneous areolar tissue and the condition known as *elephantiasis* (*q. v.*).

(*b*) *Chemical.*—Alcohol absorbed from the digestive tract and carried to the liver in the portal blood causes irritation of the hepatic tissue with increase in the periportal connective tissue and the development of cirrhosis. Lead and other chemical irritants eliminated from the body in the urine act similarly upon the kidney, provoking increase of its connective tissue.

2. **Trophic or Nervous.**—In the disease of childhood known as pseudohypertrophic muscular palsy the muscles are abnormally large, not because of any actual increase in their own tissue, but because of hyperplasia of the intermuscular fat, which is succeeded by fatty degeneration of the muscle fibers, and eventually by marked atrophy.

3. **Loss of Tone.**—When through morbid changes the bulk of any organ becomes diminished, hyperplasia of neighboring tissues occurs to compensate and fill up the gap. Thus, when one of the kidneys atrophies, hyperplasia of the perirenal fatty tissue commonly occurs to fill up the space it occupied.

4. **Excessive Nutrition from Hyperemia.**—In hyperemia of the uterus the endometrium sometimes undergoes hyperplasia. Chronic hyperemia of any organ is commonly associated with increase in its connective-tissue framework. The skin upon the hands of laborers, from the hyperemia and irritation, becomes very thick and develops callosities in consequence of hyperplasia of its epithelial layers.

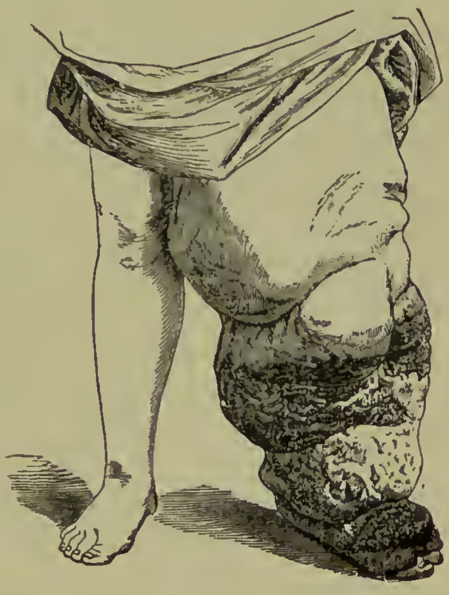

FIG. 77.—Elephantiasis of enormous development ("Barbadoes leg") (after Smith).

Morbid Anatomy.—Hyperplasia is irregular and asymmetric. In elephantiasis the form of the part may simulate the normal, but it is greatly altered in the relation of component tissues, the functional capacity being destroyed rather than increased, as in hypertrophy. In other cases, as in tumors, the hyperplasia may confine itself to no limitations of form or size, but the tissue growth may occur in every direction. Hyperplasia is readily recognized by preponderance of certain tissues which destroys the symmetry of the part affected.

Morbid Histology.—Hyperplasia can be recognized microscopically, as macroscopically, by the disproportion between the component tissue elements. The diversity of form assumed makes the recognition of hyperplasia dependent upon knowledge of the normal structure of the organ, just as its recognition by the unaided eye depends upon knowledge of the normal anatomy of the part. The striking increase in the connective tissue of the liver and kidneys in cirrhosis, the increase both in fibrous and elastic tissue in the lung in passive congestion, the encapsulating connective-tissue masses about old tubercles, gummata, abscesses, etc., cannot fail to appeal to the student as sufficiently characteristic.

Metaplasia is the transformation of a tissue into one of different type. It is illustrated in the formation of bone in the connective tissues, in the muscles in myositis ossificans, in the trabeculæ of the lung, etc., also in the fatty infiltration of the areolar tissue, by which it becomes transformed into adipose tissue. The blastodermic type of the tissue is never altered. Epithelium never becomes connective tissue, nor connective tissue epithelium.

Apparent metaplasia sometimes depends upon atrophy or necrobiosis with wasting and loss of certain structures and consequent preponderance of others.

NEOPLASMS OR TUMORS.

A tumor is a functionless and often harmful new growth, depending upon progressive hyperplasia or metaplasia of tissue. It is atypical in structure, though consisting of tissues normal to the body.

Tumors arise without apparent cause. Inflammation is unessential to their occurrence, and their structure is dissimilar to that of inflammatory lesions in that the characteristic phenomena of inflammation are absent. There is no hyperemia, no exudation, no leukocytic invasion, no granulation tissue, no cicatrization. Instead, the tissues in which the tumor develops and which surround it are entirely indifferent to its presence or show changes depending solely upon the compression or disorganization to which they may be accidentally subjected. Moreover, it is characteristic of tumors to increase and persist, while inflammations tend to recover and disappear. Inflammatory growths are always heteroplastic—that is, consist of connective tissue, regardless of the tissue or organ in which they occur; while tumors are in many cases homoplastic, or like the tissues from which they grow.

Tumors consist of tissues more or less accurately reproducing those of the normal individual either in their embryonal or adult condition, though they differ from normal tissues and organs in being heterogeneously and disadvantageously placed, in being by position and arrangement incapable of function, and in being independent of those regulating mechanisms of the body by which its parts conform to a normal morphology and act in harmony. Exemption from such regulation causes them to form actual parasitic tissue masses, living at the expense, rather than for the benefit, of the body.

Tumors differ from simple hyperplasiæ only by their more circumscribed form.

Morphology.—**Size.**—Tumors know no limitations of size except those occasioned by internal conditions, such as ability to secure nutriment for the continuous vegetative activity of their cells. Fortunately, internal conditions of malnutrition are met in nearly every tumor, precluding it from attaining excessive size. Occasionally, however, the blood supply of the tumor is rich, the cells remain healthy, and the tumor may reach a size and weight almost beyond belief, as in the case reported by Delameter, of a tumor weighing 275 pounds attached to a patient weighing only 100 pounds.

External conditions, such as ulceration and infection, may also interfere with the continuous enlargement of tumors by destroying their substance.

Shape.—The general tendency of every tumor is probably toward sphericity, but it rarely happens that it is able to grow without some kind of opposition by which its shape is modified.

A tumor mass developing within an organ and meeting with an equal opposition on all sides, as in the center of the liver, is usually spherical. Such a growth is known as a *node*.

When a tumor forms in a situation in which its growth is unimpeded except upon one side, it forms a hemispherical enlargement which is sometimes known as a *tubercle*, though this term is confusing as suggesting relationship with tuberculosis, which is not the case. A plateau-like growth well illustrated by the epitheliomata of the skin is called a *flat, tabular swelling.*

A node situated beneath the skin or a mucous or serous membrane may in the course of time become so heavy as to make traction upon its covering membrane and thus appear stalked or pedunculated, receiving the name *polyp.*

If the pedicle remain short and the node enlarge so as to overhang the base like a mushroom, the growth is called a *fungus.*

Some fungous tumors are villous or branched and justify the terms *cauliflower* or *dendritic.*

As a tumor is a "new growth," it invariably causes enlargement of the part in which it grows. Many tumors continue to enlarge and increase the size of the part affected; others, however, soon degenerate and ulcerate, and through loss of substance may cause diminution in the size of the part affected. When much inflammatory reaction occurs, cicatricial formations with contraction may further diminish the size. Such conditions occur in scirrhous tumors of the mamma and in tumors of the pylorus of the stomach, whose degenerating substance is apt to be digested by the gastric juice.

Color.—The color of the tumor depends upon the tissue or combination of tissues of which it consists. Fatty tumors are yellow; muscular tumors, grayish red; sarcomata, grayish pink; mixed tissues, such as occur in carcinoma, are variegated because of alternating pinkish tumor tissue, yellow fatty tissue, and whitish fibrous tissue. As the majority of neoplasms are badly nourished, their tissues usually appear paler than normal tissues of the same kind. Hemorrhages and retrogressive change cause them to contain dark areas occupied by disintegrating blood, brownish or yellowish areas infiltrated by blood pigment, and yellowish or whitish areas of necrosis.

The melanoma and chloroma are characterized by an abundance of metabolic pigment, by which they may vary from yellow to black. The melanoma may be coal black.

Consistency.—The consistency of the tumor depends upon its structure. Tumors of osseous and chondrous tissue are extremely hard; those of mucous tissue, extremely soft. The occurrence of mucoid metamorphosis in the tumor makes it much softer, of calcareous infiltration, very much harder, than it would otherwise be.

Number.—Tumors may be single or multiple. In most instances there is but one primary tumor, though there may be many. Large numbers of secondary or metastatic tumors may arise from a primary tumor. Sometimes malignant tumors arise independently of one another in different organs at the same time, as in both mammary glands, or in one or both mammæ and in the uterus.

Benign tumors may also be multiple, though they are entirely independent of one another. Chondromata may be numerous, especially when affecting the small bones of the hands and feet.

The most frequent multiple tumor is the *neuromolluscum fibrosum*, of which more than a thousand have been counted upon one patient.

Tumors may occur simultaneously and independently of one another, yet be of different kinds. Thus, a patient might suffer from fibroids of the uterus, carcinoma of the breast, epithelioma of the cervix uteri, etc., at the same time. Such occurrences are accidental, and cannot be interpreted as showing any special predisposition to tumor development.

Structure of Neoplasms.—All tumors correspond in structure with the embryonal or fully developed tissues of the body. The correspondence is imperfect, however, because of the rapidity of growth, irregularity of arrangement, lack of function, and tendency to degeneration inherent in all neoplasms.

Typical, *homoplastic*, or *homologous tumors* correspond in structure with the tissues from which they spring; *atypical*, *heteroplastic*, or *heterologous tumors* fail to do so. Primary homologous tumors depend upon hyperplasia, heterologous tumors upon metaplasia, of the tissues.

Neoplasms may consist of single tissues with correspondingly simple structure, or of combinations of tissue bearing a more or less complete resemblance to organs of the body. Virchow made this the basis of a classification in which the simple tissues were called *histoid* or *histioid*, and the tumors of combined tissues *organoid*. Certain neoplasms not easily referred to either class and containing derivatives of all three blastodermic layers he called *teratoid* and considered analogous to monsters.

The simple or histoid tumors consist of adipose tissue (lipoma), fibroconnective tissue (fibroma), cartilaginous tissue (chondroma), osseous tissue (osteoma), muscular tissue (myoma), mucous tissue (myxoma), and embryonal connective tissue (sarcoma).

The organoid tumors most commonly represent a very atypical gland-like structure, and all contain epithelial as well as mesoblastic tissues (epithelioma, adenoma, and carcinoma).

The teratoid tumor best known is the ovarian dermoid.

All neoplasms contain blood vessels, nerves, and lymphatics.

The *blood vessels* of tumors originate from pre-existing vessels. As the neoplasm develops without organogenetic influence, its vascularization is usually disproportionate to the requirements. In the greater number of cases the vascularization is inadequate, so that the growth of the tumor is at the expense of its nutrition, and degeneration of the older parts of the growth is inevitable. On the other hand, the vascularization of the neoplasm may be excessive, so that it is penetrated in all directions by good-sized vessels (plexiform), or contains vessels of unnecessarily large size (telangiectasis), or may contain greatly dilated blood cavities (cavernous).

The vascularization of new growths is nearly always atypical, some parts of the growth being plexiform, telangiectatic, or cavernous. other parts showing ischemia with degeneration. The excessively vascularized parts of new growths are predisposed to interstitial hemorrhages.

A common peculiarity in the vessels of morbid growths is lack of capillaries, owing to which the blood cannot properly be distributed to the tissue elements, so that early degeneration of cells, even of those close to the vessels, is inevitable.

In some cases the structure of the vessels is defective, and in sarcomata they commonly have imperfectly developed walls, and not infrequently terminate in simple channels or spaces among the cells of the tumor—a condition predisposing to the transportation of the cells of the tumor to remote regions, where metastatic growths occur.

The *nerves* of tumors are few in number and usually atypical in structure, commonly being devoid of the medullary sheaths.

The *lymphatics* of neoplasms are usually plentiful, often superabundant, and may be plexiform or cavernous.

Tumors being thus supplied with vessels, nerves, and lymphatics, it is possible for micro-organisms to be brought to them in the same manner as to other tissues, and in them the phenomena of infection, inflammation, suppuration, and other pathologic processes may take place. Repair by granulation and cicatrization may occur in tumors as in other tissues, though the atypical conditions prevailing in all neoplasms cause some aberration from the normal in whatever pathologic processes are present.

Though true that tumors usually grow from those tissues in which they occur, they differ from simple hyperplasia in that the histoid tumors are distinctly circumscribed by a surrounding "capsule." The more simple the structure of the tumor, the more distinct this capsule appears, and the more clearly the growth is differentiated from the normal tissue. Such capsules are most nearly perfect in lipomata or fatty tumors, which almost spring from the matrix when it is incised. The capsule consists in part of tissue belonging to the neoplasm itself, in part of the connective-tissue framework of the organ in which it occurs, and which has been gradually pushed aside as the tumor has grown.

The isolation of the tumor mass from its matrix by encapsulation of this kind has increased the favor with which the "embryonal rest theory" of their origin has been received.

The more completely the tumor is encapsulated, the less apt it is to do harm. Malignant tumors are either unencapsulated or have very imperfect capsules. Sometimes, as in adenoma, a part of the tumor is well encapsulated, while another part is continuous with the gland from which the tumor springs. Such tumors are apt to take on subsequent malignancy. In typical malignant tumors, such as the carcinoma, no sign of encapsulation exists.

Mode of Growth.—Tumors are said to grow either by *interstitial expansion* or by *peripheral infiltration*. All tumors grow by interstitial expansion, or the multiplication of elements throughout their substance. Benign tumors grow exclusively by this method, the malignant tumors adding peripheral infiltration. The infiltration is extremely detrimental to the infiltrated tissue, which is slowly disorganized by the invading tumor cells which grow into its interstices, fill up its lymphatic spaces, appropriate its nutriment, compress its elements, and so bring about its gradual disorganization. Tumors with a marked infiltrative tendency, though they may remain local, may invade the vital organs of the body, and, by transforming them into neoplasmic masses incapable of function, cause death.

The growth of tumors is limited chiefly by the amount of nourishment they receive. So long as they are properly nourished they increase in size; so soon as they outgrow the nutrient supply growth is checked and retrogressive changes set in.

It usually takes months or years for a simple tissue tumor to become very large, though malignant tumors may develop quite rapidly. The more simple the structure of the tumor and the less the opposition it meets from surrounding parts, the more rapidly it grows.

Retrogressive Changes.—The most frequent degeneration of tumors is mucoid metamorphosis of the connective-tissue fibers and cells. It occurs in badly nourished parts, and leads to the formation of softened areas and of colliquation cysts.

Colloid metamorphosis of the cells of epithelial tumors is frequent, and is usually recognizable macroscopically by the presence of cysts of varying size filled with the yellowish, colloid material. In ovarian cysts both colloid and mucoid degeneration may occur, or pseudomucin may be formed.

Calcification is common in tumors. It may take the form of a deposit of amorphous granules or may lead to actual bone formation (ossification). In other cases crystalline spheres and cylinders are formed, as in psammoma.

Pigmentation of tumors is frequent as the result of hemosiderin set free from destroyed red blood corpuscles after hemorrhagic extravasation. The most striking pigment found in tumors is melanin, which occurs in the malignant tumor known as melanoma or melanotic sarcoma, and may make the tissue black. Its presence is associated with a very marked malignancy. Chloroma contains a greenish-yellow pigment.

Fatty infiltration is seen in lipoma; fatty metamorphosis in the older, disintegrating parts of carcinoma.

Hyaline degeneration is seen in certain tumors, especially in cylindroma.

Necrosis is common in all tumors.

Ulceration of tumors is frequent as the result of superficial softening, of infection, and of traumatic injury with imperfect repair.

Morbid Physiology.—The growth of a tumor is entirely independent of that of the individual in whom it occurs, and takes place regardless of his physical condition. Thus, though from other causes the body may be in a condition of extreme emaciation, a fatty tumor may continue to grow, and though the fats elsewhere in the body are absorbed, the fat deposited in the tumor persists and increases. They also grow well in those whose advanced years have destroyed the vegetative activity of the normal tissues.

Tumors perform no function useful to the economy. The cells of organoid tumors with glandular structure may carry on a functional activity, but it results only in the accumulation of material which collects to form cysts.

Disposition and Tendencies.—According to their disposition, tumors are denominated *benign* or *malignant*.

A **benign** tumor is one whose inherent tendency is to remain local and do no other harm than its presence, size, or position may determine. Any injury, therefore, that follows the presence of a benign growth is to be looked upon as accidental and unexpected. Thus, a pedunculated benign tumor of the larynx, by accidentally getting caught between the vocal cords, has been known to cause death from suffocation, not, of course, because such was the tendency of the growth, but because its position accidentally permitted it. Small benign tumors of the spinal membranes may press upon the cord, occasion degeneration of its tracts, and so bring about hopeless palsy. Benign tumors of the brain may cause Jacksonian epilepsy, palsy, and even death by pressing upon important centers. Benign cartilaginous tumors of the bones may interfere with the proper movement of the limbs. Very large benign tumors may appropriate so much of the patient's blood that he is no longer able to maintain the integrity of his own tissues and also nourish the enormous mass of the tumor.

The weight of large tumors may also exhaust the strength of those who have to carry them about.

A **malignant** tumor is characterized by an inherent tendency to disorganize the tissue in which it grows, return when excised, distribute metastatic secondary growths to other parts of the body, and eventually cause the death of the patient. The injury that it inflicts upon the patient is not accidental, but is the inevitable result of its mode of growth.

Malignant tumors are, therefore, characterized as follows:

1. *A Tendency to Invade and Disorganize the Tissues.*—The malignant tumors grow in part by peripheral infiltration, their cells being unconfined by any encapsulation, penetrating into the interstices of the neighboring tissues and separating their component elements, which subsequently disappear by atrophy from pressure and malnutrition. The cells also grow into the lymphatic spaces and channels, which they fill up and obstruct. Such a tumor, therefore, has many extensions which may be compared to the roots of a tree or legs of a crab, and no doubt suggested the term "cancer," by which such tumors were first known.

2. *A Tendency to Recur when Excised.*—This peculiarity, which is known

as *recidivity*, is characteristic of unencapsulated tumors. It depends upon the continuous growth of offshoots of the tumor which are left behind when it is removed. Tumors of circumscribed form, surrounded by encapsulated connective tissue and devoid of cellular extensions into neighboring tissues, cannot recur when excised.

3. *A Tendency to Cellular Embolism, by which Secondary Growths are Started in Remote Organs.*—The cellular emboli may be very small, consisting of a cell or two, and may be transported from organ to organ either by the blood or lymph circulation. The distribution of a tumor by these means is called *metastasis*. It occurs chiefly through the lymphatic circulation in carcinoma; chiefly through the blood circulation in sarcoma.

The opportunity for metastasis is found in tumors whose cells are readily transportable because of their rounded form and loose connections, whose cells extend in prolonged extensions into the lymphatic spaces of neighboring tissues, or occur in intimate relationship with the blood circulating in the vessels.

Secondary tumors show a peculiar, more or less regular tendency to develop in certain organs, a tendency which may or may not be easily explainable. Thus, in carcinoma and epithelioma of the skin and mammary glands, as well as of the deep organs, such as the stomach, uterus, and other abdominal organs, the first metastases are to the nearest lymphatic nodes. Thoracic and mammary tumors next reach the lungs, abdominal tumors the liver, through the entrance of the cells of the tumor into the circulating blood.

Primary tumors of the pelvis ascend the retroperitoneal and peritoneal tissues, ultimately reaching the liver.

These illustrations are all easily explained by a moment's reference to the direction of the lymphatic and vascular streams into which the cells enter. It is, however, difficult to understand why melanotic sarcoma of the eye most frequently gives metastases to the liver.

The only benign tumor with a tendency to secondary colonization in remote parts of the body is the chondroma.

4. *A Tendency to bring about the Impoverished Nutrition known as Cachexia.*—Cachexia is especially characteristic of carcinoma. It is characterized by a marked secondary anemia, wasting, peculiar yellowish color of the skin, and general vital depression, and may be fatal.

It is referred by some to the pain and anxiety suffered by the patient, though it is difficult to explain how these factors can occasion the anemia, atrophy, and fatality characterizing the condition. Others feel that it must depend upon some toxic metabolic product of the carcinoma cells absorbed into the system.

Varieties of Neoplasms.—I. **According to their occurrence,** tumors are grouped as primary, secondary or metastatic, and recurrent.

A *primary tumor* is the first occurrence of the tumor. A *secondary tumor* depends upon metastatic distribution of existence of a primary tumor, and is usually dependent upon the cells. A *recurrent tumor* recurs at the original site when excised.

II. **According to their structure,** tumors are divided as follows:

A *histoid* or *histioid* tumor is one which has for its prototype a simple tissue of the body, derived from one blastodermic layer.

An *organoid* tumor imperfectly resembles some organ of the body and contains derivatives of two blastodermic layers. The structure of the tumor, usually atypical, repeats that of the epithelial glands.

A *teratoid* tumor is one which contains derivatives of all three blastodermic layers, so arranged as to suggest an imperfect embryo. The dermoid tumors (*q. v.*) are typical representatives of this class.

III. **According to their tendencies,** tumors are described as benign and malignant.

A *benign tumor* is one whose inherent tendencies are harmless and whose injurious effects depend only upon accident.

A *malignant tumor* is one whose inherent tendency is to invade and disorganize the tissue in which it occurs, recur when excised, cause the metastatic development of secondary tumors, and ultimately bring about cachexia and death.

Termination of Neoplasms.—It is said by Cornil and Ranvier that the tendency of every tumor is to increase and persist. Few if any tumors spontaneously cease to grow and disappear. Cessation of growth may occur after a time, or the growth of certain tumors may occur irregularly, progressing rapidly at one time, ceasing when the limit of nutrition is reached, then beginning growth again at some different point when accidental conditions change the balance of nutrition.

Slowly growing mammary carcinomata sometimes show fatty degeneration of the epithelial cells in the older parts, and calcification of the stroma, but in such tumors some healthy growing cells can usually be found at the periphery.

A sudden reduction in the size of a tumor usually depends upon absorption of fluid contained in a cyst formed within it. The few cases of which it is reported that small circumscribed tumors of the mammary glands have spontaneously recovered may have been errors of diagnosis, no tumors being present, but small cysts mistaken for them.

The tumors grow most rapidly in soft tissues rich in blood and lymph vessels.

Neoplasms may be fatal under the following conditions:

1. When a vital part is pressed upon by the neoplasm and its function suspended. This is particularly true of tumors of the meninges which press upon the brain.
2. When vital channels of the body are obstructed. Tumors of the abdomen sometimes obstruct the intestine, the ureters, etc. Tumors of the larynx obstruct the glottis and prevent respiration.
3. When ulceration and degeneration of the substance of the tumor cause fatal hemorrhage.
4. When secondary infection takes place through an ulcerated surface.
5. When the tumor withdraws so much blood into its own substance as to starve the affected individual.
6. When the tumor or its metastatic colonizations cause disorganization of vital organs.
7. When cachexia becomes extreme.
8. When invasion of the veins causes sudden death from embolism, as in rare cases of sarcoma.

Etiology of Tumors.—The exciting cause of tumors is unknown. Many different causes predispose to them.

1. **Age.**—Age has a marked influence upon the occurrence of tumors, those tissues tending to take on the abnormal development which are most active at the time of life at which the tumor begins its growth. Thus, the tumors of youth nearly all grow from the connective tissues. Tumors of later life, occurring after the activity of the connective tissues has ceased, are more likely to grow from the epithelial tissues. It is on this account that the surgeons are apt in cases of doubtful diagnosis to classify tumors occurring before the thirtieth year as sarcoma, those after the thirtieth year as carcinoma.

2. **Sex.**—The influence of sex upon the occurrence of tumors is marked, women being far more predisposed to them than are men, chiefly because

they possess organs, such as the mammary glands and uterus, commonly the seat of tumors, but whose homologues in men are insignificant in size and physiologic importance, and are rarely diseased.

3. **Heredity** has considerable influence, certain families being particularly liable to mammary, uterine, or gastric carcinoma, from which other entire families are free. It is only the predisposition that is hereditary, there being no evidence that the cause of the tumor passes from parent to offspring.

4. **Occupation.**—Certain occupations and habits seem to favor the occurrence of tumors; thus, a form of epithelioma of the scrotum is frequent among chimney-sweepers and paraffin and tar workers.

5. **Environment.**—According to the observations of the English, the geographic distribution of carcinoma is not uniform, cases being much more numerous in certain localities than in others.

The following theories as to the *exciting cause of tumors* have been evolved in the course of time:

1. **The Mechanical Theory of Virchow.**—This theory accounts for tumors by supposing that they result from local irritation. Many cases can be given to illustrate its probability; thus, epithelioma of the lip is more frequent in men than in women; it chiefly affects the lower lip, and it is most frequent in those who smoke clay pipes, thus appearing to depend upon the irritation of the lower lip caused by the pipe.

Carcinoma of the gall-bladder and bile ducts is in nearly all cases associated with the presence of gall-stones. Carcinoma of the stomach occurs at the pylorus, where more or less friction is said to be caused by the passage of the food. Carcinoma of the uterus is more frequent in women who have borne children than in others. Epithelioma of the cervix is more frequent in married than in single women.

In considering the situations at which the epithelial tumors develop, one finds striking examples of the fact that they nearly all occur where some particular irritation exists.

What is true of the superficial tumors is not, however, so evident of more deeply seated tumors, and as other explanations can be given to account for the occurrence of tumors at the points mentioned, it becomes doubtful whether irritation is not a rare, instead of a common, cause of tumor formation.

Keloids, it is true, occur in neglected and otherwise irritated wounds, and a form of epithelioma of the skin sometimes succeeds lupus.

Sarcoma sometimes develops subsequently to traumatic injuries, though the relationship of the injury to the tumor is not clear.

2. **The Theory of Embryonal "Rests" and "Vestiges" of Cohnheim.**—This is an endeavor to account for the origin of tumors through the displacement of fragments of embryonal tissue in the differentiating processes of embryonal life. Such groups of cells or fragments of embryonal tissue are known as "rests." They have never been recognized, so are of hypothetic existence, though the occurrence of dermoid cysts in the lines of embryonal fusion makes it probable that they originate through sequestration of some of the superficial cells. Cohnheim believed that the sequestered cells can remain latent for years, retaining the power to multiply should appropriate conditions arise. The hypernephroma of the kidney, formed by the inclusion of detached fragments of the adrenal body in the substance of the kidney, is an excellent example of such a growth.

Sutton speaks of "vestiges" as the remnants of fetal organs which fail to disappear, and in later life may occasion the formation of cysts and tumors. Among them may be mentioned the urachus, the thyrolingual duct, the postanal gut, Pflüger's tubes, etc. Cysts may form from all these by the collection of fluid within them.

The encapsulation of benign tumors, which separates them from the tissue in which they grow, is in support of Cohnheim's theory.

3. **The Nervous Theory.**—Those who hold to this view of the origin of tumors believe that the source of the trouble is to be looked for in disturbances of the trophic innervation, and that through local irregularities of nervous influence overgrowth of the tissues may take place. While it is conceivable that in some cases this may explain the development of a tumor mass, it is inconceivable that many forms of neoplasm can have such an origin, as there is no known lesion of the nerves accompanied by proliferations similar to those forming the tumors.

4. **The spermatic theory** has been entirely abandoned by modern pathologists. It taught that the cells of the body occasionally become stimulated to action through the spermatic influence of other cells that formed a symbiosis with them. This theory is entirely antagonistic to known biologic facts.

5. **The Theory of Altered Tissue Resistance.**—This theory has been earnestly supported by Ribbert, who believes that carcinoma develops not so much from proliferative tendencies on the part of the epithelial cells as from lessened resistance of the subjacent connective tissue. The theory has found little support.

6. **The Parasitic Theory.**—Many claims have been made for the importance of certain bacteria supposed by their discoverers to be specific for tumor formation. The first of these were bacteria, and most important among them was a bacillus which Scheuerlen observed and thought to be the cause of carcinoma, but which afterward turned out to be the "hay bacillus." After it had been shown that the bacteria sometimes found in carcinoma were merely accidentally present, attention was directed by Thoma, Russell, Soudakewitsch, Sawtchenko, Padwyssozki, and others to small round bodies found in the cells and regarded as protozoan parasites. These "parasites" (?) have been observed in carcinoma, epithelioma, sarcoma, myoma, lipoma, and other tumors. No two observers have, however, described exactly the same bodies, and it is very doubtful whether any of the objects described are parasites, or, if so, whether their presence is other than accidental.

Still later Plimmer revived interest in the cellular inclosures and regarded them as blastomycetes. He found them almost invariably in carcinoma, and was apparently successful in his endeavors to cultivate them and to excite neoplasm formation by their inoculation into animals. Still more recently Gaylord has returned to the protozoan theory, and described small bodies, similar and probably identical to those of Plimmer, as protozoan parasites.

One of the great difficulties is our inability to reproduce the disease in the lower animals by the transplantation of "grafts." Those suffering from carcinoma readily inoculate themselves and can readily be experimentally inoculated, but healthy persons cannot be successfully inoculated with tumor tissues taken from others.

Though the parasitic theory of tumors is very attractive, and while many of the apparent difficulties in the way of its acceptance may ultimately be explained away by the demonstration that the parasite is one which lives but part of its existence in man and another part in some lower animal, its demonstration at the present time is far from complete.

In truth we are no nearer the correct solution of the etiology of tumors, so far as any accurate knowledge of the parasites is concerned, than we were ten years ago.

The inoculation of tumor tissue has succeeded in the hands of Hanau and Mayet and Loeb, although Alibut, Shattuck, Ballance, and many others worked extensively upon the subject without result. Plimmer produced connective-tissue hyperplasiæ resembling tumors by the inoculation of pure cultures of a yeast (?) which he isolated from a carcinoma and supposed to be a form of the "Plimmer body" well known in the carcinoma cells. Gaylord claims similar results. None of the growths was identical with those from which the supposed parasites were cultivated.

Hanau was successful in transplanting an epithelioma of the vulva of a rat to other rats, and Loeb has successfully transplanted a cystosarcoma of a white rat from white rat to white rat for many generations, but with these exceptions inoculation experiments, even on a scale as thorough as those of Shattuck and Ballance, who introduced entire tumors into the peritoneal cavities of the larger lower animals, fail to produce any neoplasm formation.

Classification of Tumors.—No classification has yet been devised that has been sufficiently satisfactory to meet with universal approval. Two bases of classification are usually adopted, the result being either an embryologic or a histologic classification, or, what is very undesirable, a combination of both. The best embryologic classification is the following, devised by Adami:

I. LEPIDOMATA OR "RIND" TUMORS.

A. PRIMARY LEPIDOMATA.

1. EPILEPIDOMATA.

Tumors whose characteristic constituents are overgrowths of tissue derived directly from the epiblastic lining membranes, or true epiblast.

(*a*) *Typical.*—Papilloma and epidermal adenomata (of sweat, salivary, sebaceous, and mammary glands, etc.).

(*b*) *Atypical.*—Epithelioma proper and carcinoma of glands of epiblastic origin.

2. HYPOLEPIDOMATA.

(*a*) *Typical.*—Adenoma and papilloma of the digestive and respiratory tracts, thyroid, pancreas, liver, bladder, etc.

(*b*) *Atypical.*—Carcinoma developing in the same organs and regions.

B. SECONDARY LEPIDOMATA.

3. MESOLEPIDOMATA.

Tumors whose characteristic constituents are cells derived in direct descent from the persistent *mesothelium* of the embryo.

(*a*) *Typical.*—Adenoma of the kidney, testicle, ovary, urogenital ducts; adenoma of the uterus and prostate; adenomata originating from the serous membranes, "mesothelioma" of the pleuræ, peritoneum, etc.

(*b*) *Atypical.*—Cancer of the above-mentioned organs; squamous endothelioma, so called, of serous surfaces, epithelioma of the vagina.

4. ENDOTHELIAL LEPIDOMATA.

Tumors originating from the endothelium of the blood and lymph vessels; endothelioma and perithelioma.

II. HYLOMATA OR "PULP" TUMORS.

1. EPIHYLOMATA.

Tumors whose characteristic constituents are overgrowths of tissue derived from the embryonic pulp of epiblastic origin.

(*a*) *Typical.*—True neuroma and glioma.

(*b*) *Atypical.*—"Gliosarcoma."

2. HYPOHYLOMATA.

Tumors derived similarly from embryonic pulp of hypoblastic origin.

(?) Chordoma.

3. MESOHYLOMATA.

A. Mesenchymal Hylomata.—Derived from tissues originating from the persistent mesoblastic pulp or mesenchyme.

(*a*) *Typical.*—Fibroma, lipoma, chondroma, osteoma, myxoma, and leiomyoma.

(*b*) *Atypical.*—Sarcoma (derived from mesenchymatous tissues) with its various subdivisions—fibrosarcoma, spindle-cell sarcoma, oat-shape-cell sarcoma, chondrosarcoma, osteosarcoma myxosarcoma, melanotic sarcoma, etc.

B. Mesothelial Hylomata.—Tumors which are overgrowths similarly of tissues derived from embryonic pulp of definitely mesothelial origin.
Rhabdomyoma.

This system is extremely convenient, but involves the use of an entirely new terminology not yet incorporated in the text-books or adopted by teachers, so that its use at present might serve to confuse rather than to elucidate the subject.

The student can easily grasp the force of a histologic classification, however, and the following is recommended:

A. Histoid Tumors. Tumors of the Connective Tissues.

I. *Composed of unspecialized tissues.*	
(*a*) Of embryonal type	Sarcoma.
(*b*) Of adult type	Fibroma, Lipoma, Myxoma, Osteoma, Chondroma.
II. *Composed of specialized tissue.*	Myoma, Glioma.
III. *Composed of combinations of simple tissues*	Angioma, Lymphangioma, Lymphadenoma.

B. Organoid Tumors. Tumors of the Epithelial Tissues.

I. *Characterized by nerve fibers and cells*	Neuroma.
II. *Characterized by surface epithelium.*	
(*a*) Squamous	Papilloma, Epithelioma.
(*b*) Columnar	Papilloma, Epithelioma.
III. *Characterized by glandular cells.*	
(*a*) Conforming to the normal type	Adenoma.
(*b*) Not conforming to the normal type	Carcinoma.

C. Teratoid Tumors.

I. Composed of connective tissue and epithelium	Cholesteatoma, Dermoid.

TUMORS OF THE CONNECTIVE TISSUES.

I. Composed of Tissue of Embryonal Type.

SARCOMA.

A sarcoma is a tumor consisting essentially of cells similar to those of embryonal connective tissue. All sarcomata develop from mesoblastic cells. A sarcoma does not consist of embryonal tissue, for such a tissue would ultimately perfect its growth, which the sarcoma tissue never does. From its beginning a certain type of round- or spindle-cell structure persists, the cells not transforming to perfectly developed tissue.

The types vary greatly: certain forms are made up exclusively of round cells; others of spindle cells; others of spindle cells and fibers. The spindle-cell sarcoma, which represents the more advanced stage of connective-tissue development, does not, however, pass through the round-cell stage, but is composed of spindle cells from the very beginning.

The sarcomata are composed essentially of cells, between which a very small amount of intercellular substance, usually of a fibrillar form, is present. As a rule, this intercellular tissue is comparatively insignificant, and is seen with difficulty. In the round-cell sarcoma it is usually granular; in the spindle-cell form reticular.

Sarcoma grows by infiltration, so that in addition to the universal interstitial expansive growth by multiplication of the cellular elements, the periphery of the tumor is not sharply circumscribed from the surrounding tissues, and the growing cells constantly penetrate the contiguous tissue, extending into the spaces among its component cells, and leading to its ultimate disorganization.

Sarcomata, especially the spindle-cell variety, are occasionally encapsulated. They are usually very poorly provided with blood vessels, though the similarity between sarcoma tissue and granulation tissue would suggest that the tumor should contain rich vascular plexuses. The circulation of the tumor is, therefore, chiefly capillary.

Not only are the blood vessels few, but in many cases those present are also imperfect in structure, consisting of an endothelial coat with a few supporting connective-tissue fibers and occasional muscle cells. Considerable parts of the tumor may be entirely without blood vessels, but contain sinuses or clefts, through which the blood circulates through the spongy tumor substance. In rare instances, and not infrequently in circumscribed areas of large tumors, the reverse condition may be true and an unusual vascularity exist. Such tumors are described as telangiectatic, cavernous, or hemorrhagic, as the case may be. The size of the vessels may be so great as to make the tumor pulsate.

Excessively vascular sarcomata are known as *angiosarcomata.*

Sarcomata are usually devoid of lymphatic vessels.

Seat of Occurrence.—The tumors originate from the cells of the connective tissues, and are, hence, of almost universal distribution. Indeed, there is scarcely any tissue or organ of the body in which a sarcoma may not develop. Sarcomata have been observed in the skin, subcutaneous tissue and fascia, subserous connective tissue, choroid, marrow of the bone and periosteum, dura mater, pia mater of brain and cord, lymph nodes, adventitia of blood vessels, nerve sheaths, submucous tissue, ovary, and uterus. Sarcoma is a somewhat rare primary tumor of organs, though secondary sarcomata in the organs are common.

Etiology.—The sarcoma is a tumor of youth and early adult life. It is sometimes congenital and occurs at all ages from infancy to extreme old age. Its cause is unknown. A few observers have claimed to find in and among the cells of the tumor certain parasitic protozoa, but nothing definite is known of the nature of these bodies. A few cases appear to follow traumatism, but the majority occur independently of any recognizable cause.

Morbid Anatomy.—Sarcomata usually form rounded, more or less lobulated, and irregular tumors, which may form nodes, either imbedded, sessile, pedunculated, or pendulous. They may be encapsulated, and are nearly always rather well circumscribed, though this depends upon the form, the infiltrating round-cell sarcoma being without sharp demarcation from the surrounding tissue. Upon section the tumors are usually pinkish gray in color and for the most part homogeneous, though this will depend upon the variety, as will be shown below. The appearances are further modified by the presence of degeneration, irregularity of vascularization, and other local conditions. The melanotic sarcoma is easily recognized by its color.

Pathologic Histology.—The sarcoma consists essentially of cells, varying in the different forms. Whether round, spindle, or irregular in shape, the cells are characterized by the presence of large rounded or ovoid vesicular nuclei, rich in nuclein, and by a relatively small amount of cytoplasm. Mitotic figures are numerous and beautiful in rapidly growing tumors, while nuclear abnormalities, such as *hyperchromatosis, karyorrhexis,* and *karyolysis,* are frequent. A small amount of homogeneous granular or fibrillar intercellular substance is always present, but may occur in such relatively small quantity as to be entirely overlooked. The cells are in intimate association with the intercellular substance, and in penciled or brushed specimens do not readily fall away, being held by delicate protoplasmic prolongations.

Retrogressive Degenerations.—The irregular blood supply makes retrogressive degenerative conditions exceedingly common. Only those degenerations are observed which affect connective tissues, the most frequent being mucous or *myxomatous* degeneration. Some of the tumors seem to degenerate almost as rapidly as they form; others degenerate locally as their nutrition fails. To both forms the term myxosarcoma is applied. Tumors are frequently *pigmented*, either with hemosiderin or melanin. The hemosiderin results from the destruction of red blood corpuscles after interstitial hemorrhage, to which the imperfect vessels of the tumor predispose; melanin, the more common pigment, from metabolic activities of the cells.

Disposition.—The sarcomata vary through all degrees of malignancy. Some are certainly and rapidly fatal; others liable to recur after excision or amputation; others remain purely local and disorganize the tissue in which they grow; still others are on the border-line of benignancy. Soft, moist tumors are more apt to be malignant than firmer and more fibrous tumors. All tend to recur after excision, and the majority to produce secondary growths by metastasis. Metastasis is most frequent in the melanotic, round-cell, lymphoid, and large spindle-cell varieties. The small spindle-cell and giant-cell sarcomata recur locally, but are less apt to be metastatic. The metastasis of sarcoma takes place almost exclusively through the blood channels, and is most rapid when the blood circulates in indefinite spaces in the tumor and is free to detach and transport the cells to other parts of the body. Lymphatic metastasis is rare because the tumors contain so few lymphatics. Sarcomata of the skin, mucous membranes, testicles, tonsils, lymph nodes, and fascia may, however, give metastasis to the lymph glands.

Small round-cell sarcomata of the femur and maxilla are usually fatal within a year. Sarcoma of the kidney rarely permits the patient to live longer than a year.

Sarcomata show a remarkable disposition to invade and grow into the veins, sometimes forming masses several centimeters in length, growing in the interior of the larger veins, though still attached to the parent tumor and vascularized from it. Such extensions sometimes break off, and if large, may cause fatal embolism.

Sarcoma may become almost universal in its metastatic distribution, appearing as minute scattered foci over the entire abdominal viscera, etc., when it is known as *sarcomatosis*.

The rapidity of growth in sarcoma seems to depend upon the character of the cells as well as upon their nutrition. The round-cell tumors grow most rapidly, especially when highly vascular.

SPECIAL VARIETIES OF SARCOMA.

Round-cell Sarcoma.—A round-cell sarcoma is composed exclusively of round cells, between which a few fibrils of intercellular substances are present. The round-cell sarcoma represents the earliest stage of embryonal connective tissue. It is one of the common tumors, and according to Sutton, is almost "ubiquitous" among vertebrate animals.

Morbid Anatomy.—The tumors are usually of small size and are rarely encapsulated. When a freshly cut surface is carefully examined, it is found to have a semi-translucent, homogeneous consistency, resembling brain substance, and a white or grayish-pink color. The tissue is not very firm, is usually friable, and when scraped with a knife gives up a creamy substance in unlimited quantity. The longer and harder one scrapes, the greater the amount of creamy material he can collect. In fact, by thus scraping with a sharp instrument the cells of the tumor are simply detached from one another, and the tumor is little by little scraped away.

Pathologic Histology.—The cells are spherical, each being provided with a deeply staining large vesicular nucleus, which occupies its center. In sections it is often with difficulty that the student can define the delicate colorless cytoplasm surrounding the nucleus. By actual measurement the cells are found to be a little larger than lymphocytes. Between the cells occasional fibrilla can be seen, but the tumor is composed so entirely of cells that it seems held together solely by their cohesion.

The tumor is most frequent in the subcutaneous tissues, but may occur in almost any part of the body. It is highly malignant, nearly always leading to a fatal termination, life not being prolonged more than a year or two in most cases. The secondary growths occur in the lungs, liver, spleen, kidney, and other organs.

Occasional small round-cell sarcomata bear a close resemblance to the structure of lymph nodes—that is, between the sarcoma cells a connective-tissue reticulum with branched and stellate cells is present. This form is described as *lymphosarcoma* or *lymphadenoid sarcoma*. Its macroscopic appearance is identical with that of the small round-cell sarcoma, but its distribution is rather more limited. It most frequently occurs in the mediastinum, in the subpleural and subperitoneal connective tissue, at the base of the tongue, in the tonsils, and in the testes.

In disposition the two tumors are similar, both being highly malignant and usually fatal.

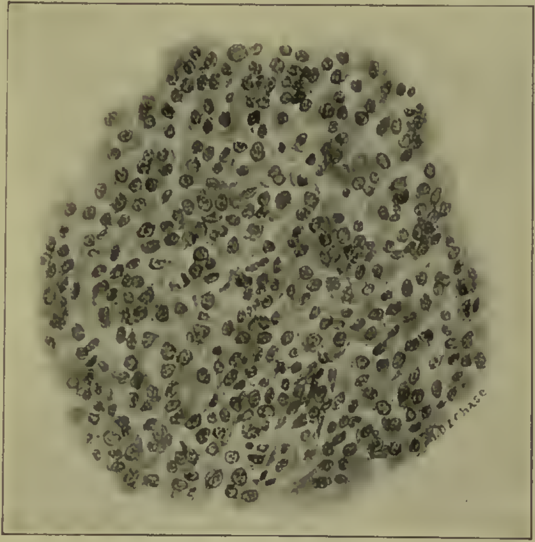
FIG. 78.—Small round-cell sarcoma of the lower jaw. Oc. 3; ob. D. D.

Large Round-cell Sarcoma.—The cells of the round-cell sarcoma may be usually large, and sometimes unequal in size. Tumors composed of such cells are called *large round-cell sarcomata*. They occur in the motor apparatus, the skin, ovary, testicle, and lymphatic nodes. In general their appearance is similar to that of the ordinary form, but they are less soft and not so much creamy material can be scraped from them. In addition to the large size of the cells, the microscope shows considerably more intercellular substance, so that a distinct network of fibers may intercept the cells. The intercellular substance itself not infrequently contains cells of the connective-tissue type, which contrast with the large round cells of the tumor. An alveolar arrangement of the cells is common. The cells are not always round, but may be faceted or even attenuated.

The clinical characteristics of the tumor in general resemble those of the small round-cell form, but it is the less malignant. It is said by Payne that the secondary growths of spindle-cell sarcoma sometimes assume this form.

Spindle-cell Sarcoma.—A spindle-cell sarcoma consists exclusively of spindle cells. The tumor is of frequent occurrence, and Warren considers it to be the most common form of sarcoma.

Morbid Anatomy.—The tumors vary much in size, some becoming no larger than an egg, others much larger, in some cases attaining the size of a man's head, and in rare cases still larger dimensions.

They are sometimes circumscribed, rarely distinctly encapsulated, but invade the surrounding tissues in all directions. On section they appear pink or grayish in color, slightly mottled, and glistening. They are not quite so homogeneous in appearance as the round-cell variety, and at times it is possible to make out with the naked eye the direction of the cellular bundles forming the tumor. When the tumor is scraped the spindle cells detach less readily than the round cells, and the knife does not collect so much creamy pulp as from the round-cell sarcoma. This probably depends upon the greater cohesive surface afforded the elongate cells.

Pathologic Histology.—The cells may be oval or oat-shaped, or may be elongate like epithelioid cells, or at times extremely long, so as closely to resemble the unstriped muscle cells. As a rule, the cells are arranged with their long diameters parallel. In very soft tumors, however, they may be irregularly arranged. Each cell has an oval vesicular nucleus, which stains intensely. The tumor is made up of bundles of cells arranged parallel, passing in and out among one another. The result of this arrangement is that in all sections of such tumors one is apt to find cells cut longitudinally, obliquely, and transversely. Islets of cartilage are frequent in spindle-cell sarcoma, tumors containing them being known as *chondrifying sarcomata*. Bony spicules also commonly occur in parosteal and periosteal sarcomata, which are then known as *ossifying sarcomata*.

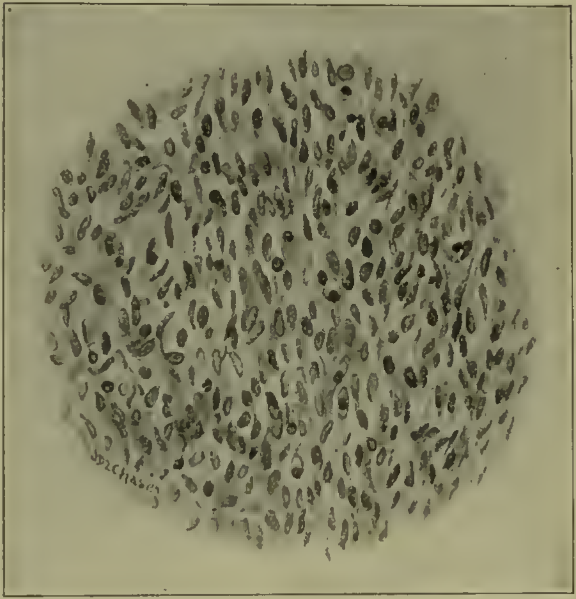

FIG. 79.—Spindle-cell sarcoma of the mammary gland. Oc. 3; ob. 9.

These tumors represent a later stage of granulation tissue than those composed of round cells.

When the cells are closely packed together, it may be impossible to make out their individual limits, though the student can usually find detached cells at the edges of the section of tissue. If intercellular substance be present in spindle-cell sarcoma, it is in very small amounts, and is not at all apparent when ordinarily examined. Mallory's method of staining connective-tissue fibers defines a reticulum, however, where it cannot otherwise be seen.

Sometimes a considerable amount of fibroconnective tissue can be seen between the cells. Tumors with this structure being dense and hard, are properly termed *fibrosarcoma*.

The spindle-cell sarcomata are more likely to contain blood vessels than the round-cell varieties. The cells usually surround them as a kind of mantle, or the blood vessels pass between encircling bundles of cells. The cells of some of the tumors are uniformly small, those of other tumors uniformly larger and sometimes very much larger. This leads to division of spindle-cell sarcomata into two classes, composed respectively of *small* and *large* spindle cells.

Among the spindle cells multinucleated cells are not infrequently found, and giant cells are more common than in any other form of sarcoma. Occasionally stellate and irregular cells are observed.

The tumors grow from various connective tissues, such as fascia, subcutaneous and submucous tissues, intermuscular septa, periosteum, and from the fibrous tissue of glands, especially the mammary gland. They are firmer than those of the round-cell variety, and may even approach to fibroma in hardness.

The spindle-cell sarcoma is malignant, its malignancy varying according to the size and looseness of the cells. Thus, the small spindle-cell sarcoma is less malignant than the large spindle-cell sarcoma, and the fibrosarcoma least so. The circumscribed and encapsulated tumors are also much less malignant than the infiltrative form. The malignancy consists in destructive infiltration of the tissue in which they grow, in recurrence after excision, and in metastasis.

Spindle-cell sarcomata are less prone to give metastasis than are the round-cell sarcomata, probably because the shape of the component cells and length of attached surface between each and its neighbor lessen the facility with which they can be torn loose and transported, and probably explains why the fibrosarcoma, in which the cells have scarcely any freedom, is the least malignant form.

Paget called these tumors *recurrent fibroids*, and Lembert spoke of them as *fibroplastic tumors*. In the mammary gland they not infrequently contain cysts which seem to depend upon the presence of included portions of the glandular substance in the sarcoma. These acini or ducts dilate, forming cysts, into which the sarcoma tissue subsequently grows, transforming them into narrow spaces, which appear in sections like the canaliculi of the gland. The tumors are seen only in the mammary and other glands, and in their secondary growths the canaliculi with their epithelial linings are absent.

Giant-cell or Myeloid Sarcoma.—A giant-cell sarcoma is one composed of spindle cells or of round cells, but containing many giant cells.

Seat of Occurrence.—These tumors occur most frequently in connection with the osseous system, where they occur as central tumors, usually of the long bones, especially the upper end of the tibia and lower end of the radius. Because of their situation they usually attain a large size before attracting attention to themselves, and because of their deep-seated position are frequently permitted to remain until inconvenience necessitates operation.

Morbid Anatomy.—The tumors arise from the medulla of the long bones, and are frequently encapsulated and distinctly circumscribed. They vary from moderate softness to distinct firmness in consistence, are reddish brown or maroon in color upon section, and have a somewhat fibrous appearance. The difference between spindle-cell sarcoma and giant-cell sarcoma cannot always be made out with the naked eye.

The origin of the tumor from the marrow of the bone gives it the name *myeloid sarcoma*, by which it is often known.

Pathologic Histology.—The giant cells may be few and small or large and numerous. They may be present in certain parts of the tumor only. It is not unusual to find them containing as many as 100 nuclei. They are circumscribed in outline, and the peripheral portion of the cytoplasm is free from nuclei, which gather together in a mass in the more central part. Inasmuch as the nuclei of spindle cells are oval in form, it is only natural that the nuclei of the giant cells of this form of sarcoma should also be oval. The nuclei of the giant cells usually have their long diameters parallel.

The formation of the giant cells is not clear. In the round-cell sarcoma the giant cells appear to be formed by karyokinesis of nuclei without division of the cytoplasm. This may also be true in some cases in which the giant cells occur in spindle-cell sarcoma, but this explanation will not suffice for all cases, for if one closely examines the spindle cells near the giant cells of such tumors, it will usually be found that their cytoplasm is in an unhealthy condition and that there is more or less widespread tendency to degeneration, which can scarcely be correctly termed hyaline, though the cells appear unusually transparent and become unusually viscid. This viscidity seems to be the key of the situation, as it permits confluence or fusion of the cytoplasm of neighboring cells, with the resulting formation of multinuclear masses or giant cells.

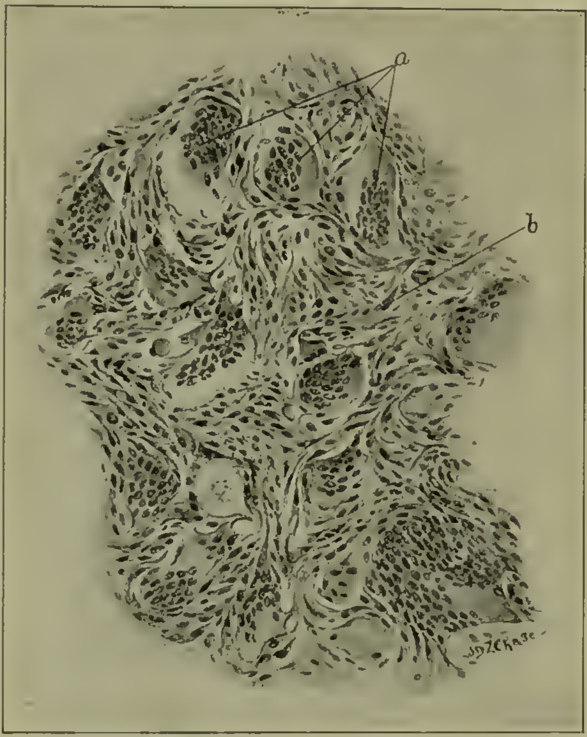

FIG. 80.—Giant-cell sarcoma of the thigh: *a*, Giant cells; *b*, spindle cells.

The giant-cell sarcoma is the most benign form of sarcoma. It disorganizes the tissue in which it grows and sometimes recurs after excision, but the occurrence of metastasis is rare.

The bones most likely to be affected are long bones, the tumor usually developing from the cancellous tissue at the extremity. The most usual situation is the lower end of the femur and upper end of the tibia. As the tumor grows the bone is invaded and eroded, and sometimes made porous, so as to be unusually liable to fracture. Sometimes it grows from the periosteum, this being especially common upon the jaw, where the tumor is called an *epulis*. The external dimensions of the tumor give no evidence of the extent to which the marrow cavity and cancellous structure of the bone may be invaded, so that surgeons in operating find it expedient to remove the entire diseased bone and amputate at a joint rather than to excise the tumor or perform a partial amputation.

MISCELLANEOUS FORMS OF SARCOMA.

Some sarcomata receive special names from other characteristics.

Multiple Myeloma.—The multiple myeloma is a tumor developing from the red bone marrow, characterized by multiple primary occurrence, chiefly upon the sternum, ribs, vertebræ, and skull, and tending to replacement of the bone by tumor tissue. It has been variously described as angiosarcoma, lymphosarcoma, lymphadenia ossium, and general lymphadenomatosis. It was first called multiple adenoma by J. von Rustizky. It is a rare tumor, only about 20 cases having been recorded. The clinical features with which it is associated are peculiar in resembling progressive pernicious anemia. The urine nearly always contains considerable albumose, and sometimes a small quantity of albumin. Asthenia is usually marked, there is considerable pain, and death takes place slowly, sometimes preceded by unconsciousness. For these reasons some pathologists have come to look upon the disease as related to leukemia, and have described it as a form of pseudoleukemia.

Pathologic Anatomy.—The tumors are multiple. The sternum and ribs are usually affected; sometimes the vertebræ and skull. The tumors are dark red in color, like the red bone marrow, nodular in form, and soft in consistence. Large tumors of this kind are occasionally pulsatile. The osseous tissue appears to be absorbed.

Pathologic Histology.—The tumor is composed essentially of cells which have usually been described as lymphocytes, but which Wright describes as identical with Unna's plasma cells, which are normal components of the bone marrow. According to Wright, the tumors do not grow from the bone marrow as a whole, but depend upon proliferation of the plasma cells. The tumor is made up of dense aggregations of these cells with wide blood spaces without definite walls, and an intercellular substance consisting of fine fibers. The old bone melts away before the growing tumor, scarcely any new bone being formed, so that the tumor soon reaches the periosteum, which it first infiltrates, then involves the contiguous tissues.

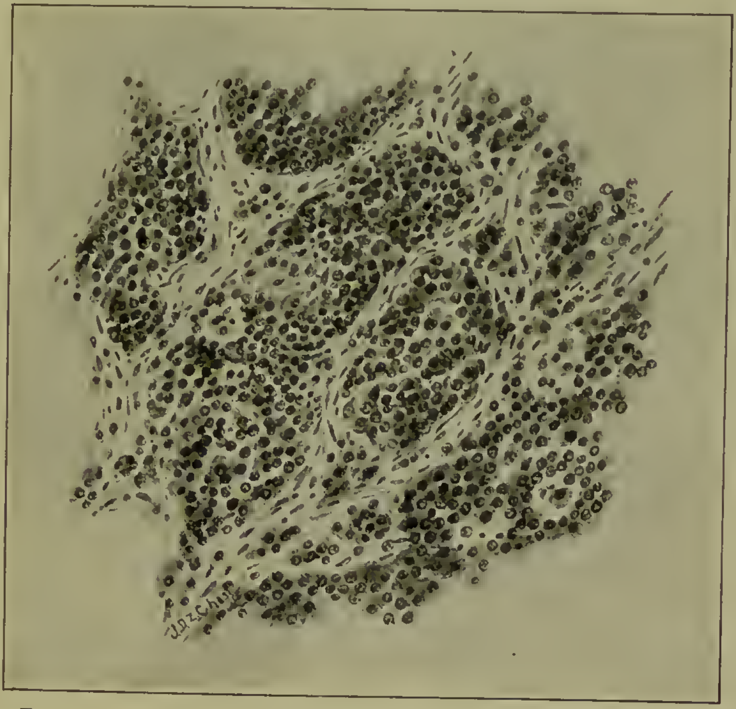

FIG. 81.—Alveolar small round-cell sarcoma. Zeiss, Oc. 4; ob. c.

There are no distinctive blood changes associated with the disease. In Wright's case there were 4,700,000 red and 5000 white blood corpuscles and 60 per cent. of hemoglobin.

Alveolar Sarcoma.—This is a round- or spindle-cell sarcoma divided into larger or smaller cell masses, separated from one another by intermediate bands of fibrillar or cellular tissue, forming a reticulum. It is the alveolar appearance which characterizes it. An alveolar arrangement may be simulated in rapidly infiltrating sarcomata, but is then observed only at the periphery of the tumor. In the true alveolar sarcoma the typical arrangement extending throughout all parts of the tumor characterizes both primary and secondary growths. The partitions consist of well-formed fibers of connective tissue. The blood vessels of the tumor may be few or many, well developed or poorly developed, and are usually found in the fibroconnective-tissue bands, ramifying throughout its structure.

In rare cases the partitions consist entirely of cells like those seen in spindle-cell sarcoma. These cells may form the reticulum in a round-cell sarcoma, but one must be careful in observing tumors of this kind lest he mistake for round cells the transverse sections of spindle cells.

The alveolar sarcoma is said to be highly malignant. It is difficult to explain why this should be the case, unless the alveolar appearance simply signifies that the tumor has a rapidly infiltrating character. The tumors may have frequently been confounded with carcinoma, to which they sometimes bear close resemblance. Certain characteristics, if well marked, will aid in a differential diagnosis; thus, the lymphoid character of the sarcoma cells, the nature of the tissue from which the tumor originates, the staining property of the nuclei, etc., may be positive aids, though in many cases they fail. Especially is this the case in the form of alveolar sarcoma known as *endothelioma*.

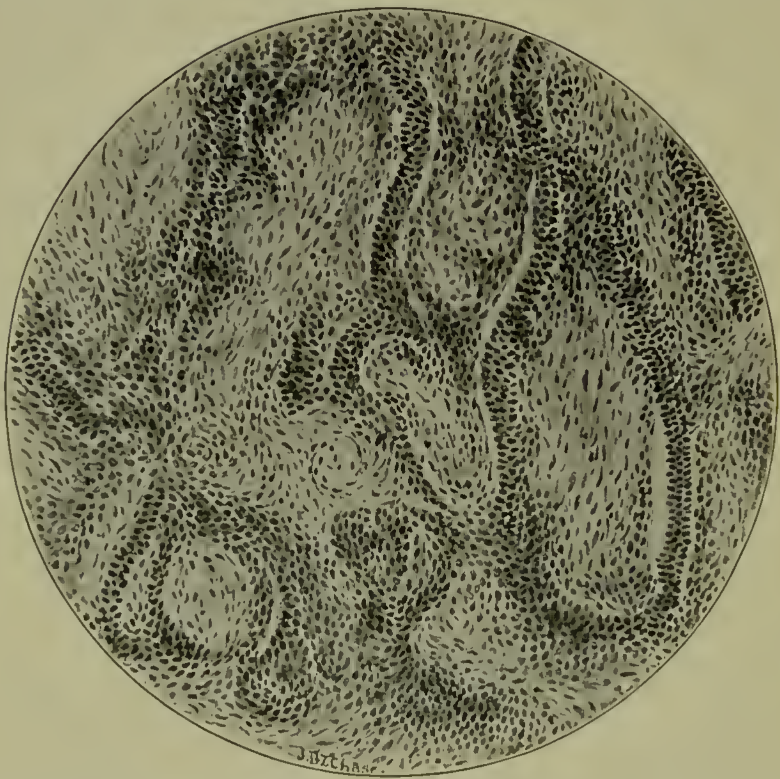

FIG. 82.—Endothelioma of the pleura. (Zeiss, Oc. 2; ob. c.) The illustration shows the cellular growth in the form of cylindric masses which fill crevices of the tissue, probably originally lymphatic channels.

Alveolar sarcoma frequently originates from the skin, but may grow from the bones, lymphatic glands, and pia mater. In the skin its development usually takes place from pigmented moles and warts. It also occurs not infrequently from the serous membranes, notably the pleura and peritoneum, in both of which situations it is called endothelioma.

Endothelioma.—The endothelioma is a tumor originating from endothelial cells. It occurs in the membranes of the brain and spinal cord, pleura, peritoneum, lymphatics, testicle, liver, ovary, brain, parotid gland, and skin.

Morbid Anatomy.—Macroscopically, the tumors form more or less circumscribed, flattened, firm, grayish-white growths, with many auxiliary growths and frequent prolongations in the direction of the lymphatic current. Upon section they present a mottled, granular appearance resembling carcinoma, and depending upon alternating nests of cells and intermediate fibrous bands. This appearance is characteristic of alveolar sarcoma and not peculiar to endothelioma alone.

Pathologic Histology.—In its early development the tumor consists of a fibrous stroma, formed, at least in part, of the tissue in which the tumor grows. In the spaces in this matrix are numerous cell nests with branched extensions, highly suggestive of carcinoma nests, but not always clearly differentiable from the cells of the surrounding connective tissue. These cells can be classified as endothelial cells only by careful inspection. Their resemblance to epithelial cells is sometimes great, and reliance must not be placed upon the microscopic appearance solely, but in all cases attention must be paid to the origin of the tumor and the tissue in which it develops. The endothelial cell nests are apt to be arranged in parallel columns or in a plexiform manner. The relation of cells to connective tissue is very intimate, and the tubules are apt to inclose some leukocytes.

Endothelioma is malignant, though slowly metastatic.

Melanotic sarcoma, melanosarcoma, or **melanoma** is any form of sarcoma whose cells are pigmented with melanin. Any variety of sarcoma may thus be pigmented. The pigment (melanin) is brown or black in color, and occurs in the form of amorphous granules, which are partly within the cells (chromatophores) and partly between them. The cells may be almost entirely destroyed by the pigmentary degeneration and appear as aggregations of granules, recognizable as cells by their shape only. Pigmentation occurs in all parts of the cell. Together with the melanin, hemosiderin may be found, and doubly pigmented tumors of this kind are not rare. The melanin is usually contained within the cells: the hemosiderin both within and between them.

Seat of Occurrence.—The tumors occur in the skin, choroid coat of the eye, and ciliary body.

Morbid Anatomy.—Macroscopically the tumor is characterized by its dark color. Cut sections may be yellowish brown, brown, or black. The pigmentation may be uniform or mottled, or parts only of the tumor may be pigmented.

Occasionally the primary tumor is deeply pigmented; the metastatic tumors pale. Sometimes the primary tumor may be quite pale and contain very little melanin, though its secondary tumors may be black. If many deeply pigmented tumors are present, the skin of the patient may become dark (*melanosis*).

Melanotic sarcoma is highly malignant, causes early metastasis, and is commonly fatal. Melanotic tumors of the eye have their most frequent metastasis in the liver.

Myxosarcoma.—All sarcomata are particularly prone to undergo mucous degeneration, with the formation of irregular cavities filled with mucus. As ordinarily seen, myxomatous degeneration depends upon malnutrition of the tissue, but occasionally the myxomatous degeneration cannot be explained, and seems to occur simultaneously with the growth of the tissue and to be present everywhere. Both of these conditions may prop-

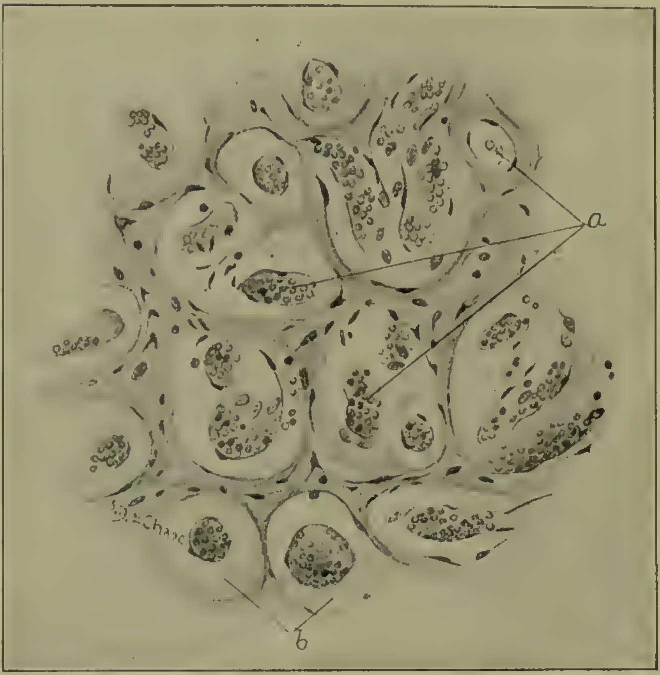

FIG. 83.—Cylindroma from membranes of the brain: *a*, Blood vessels; *b*, hyaline cylindric encasements of blood vessels.

erly be described as myxosarcoma. Occasionally the mucous degeneration causes a peculiar appearance in microscopic sections, as in cylindroma.

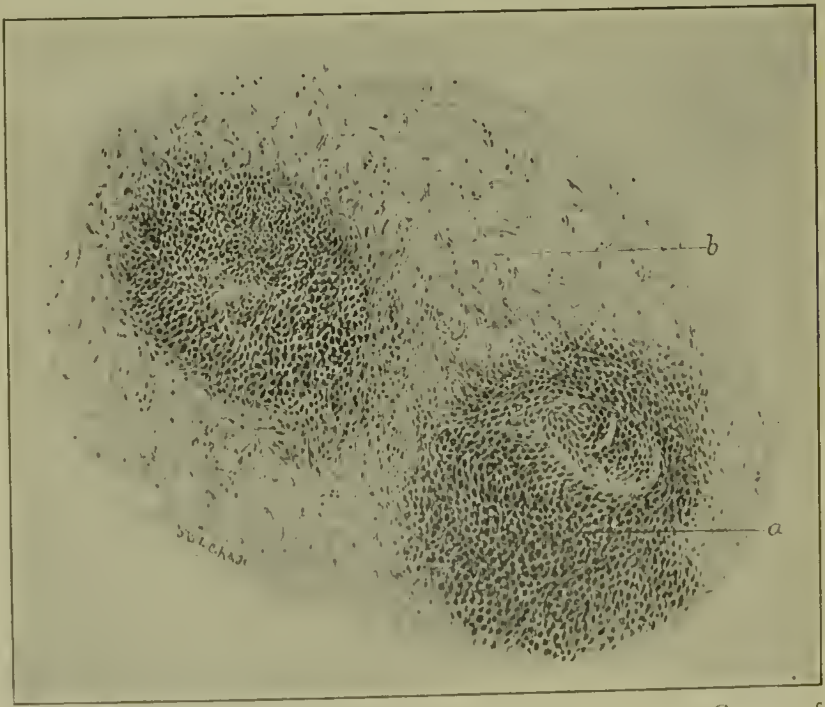

FIG. 84.—Myxangiosarcoma tubulare (perithelioma (?)) of the ovary: *a*, Groups of healthy cells surrounding blood vessels; *b*, mucous degeneration of matrix of tumor.

Cylindroma is characterized by a mucous or perhaps sometimes hyaline degeneration, occurring in the walls of the blood vessels or in cells contiguous to them. It is seen only in angiosarcoma, and is characterized by the presence of hyaline cylinders about the blood vessels. Such tumors are usually soft and white and rich in cells, though when the degeneration is marked, a few cells may be present between the hyaline cylinders.

Macroscopically the tissue has a peculiar translucent quality, and a cloudy mucus can be scraped from the cut surface. The tumor is also sometimes known as plexiform angiosarcoma myxomatodes. It usually occurs in the brain and its membranes, the orbit, the jaw, and the peritoneum.

Myxangiosarcoma Tubulare.—In other cases the myxomatous degeneration affects all the cells of the tumor except those in close contact with the blood vessels of angiosarcoma, a condition exactly the opposite of that seen in cylindroma. The microscopic picture is strikingly characteristic, for when the section is examined with a low-power lens, scattered over the field one finds transverse and oblique sections of blood vessels, surrounded by cells in a condition of fair nutrition, the appearance somewhat suggesting *Malpighian* corpuscles in the spleen. The remainder of the tumor consists of cells whose outlines only can be seen, or simply the remnants of a tissue, evidently at one time largely composed of cells, but now destroyed by mucous degeneration. This form of tumor is described as *myxangiosarcoma tubulare.* The tumors are very soft and mucus escapes from them when incised; the disposition is extremely malignant. They are rather common in the eye, the ovary, and the peritoneum.

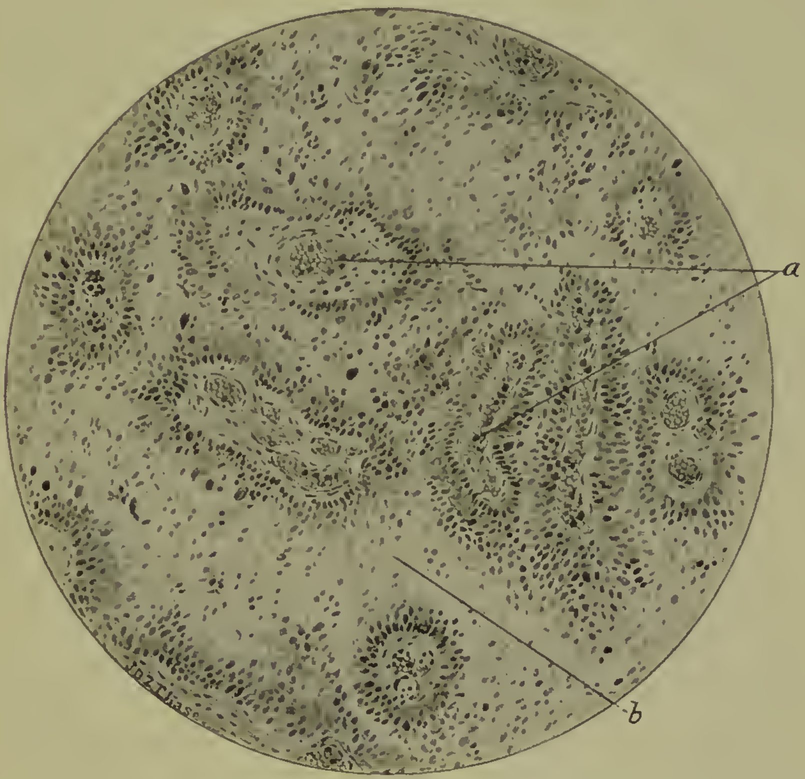

FIG. 85.—Perithelioma of the retina: *a*, Blood vessels surrounded by cells in a good state of preservation; *b*, degenerated portion of tumor.

Perithelioma.—Tumors with healthy cells about blood vessels, contrasting with destroyed cells or an acellular tissue elsewhere, have recently attracted considerable attention under the name of *perithelial sarcoma*, a name given because of their supposed origin from the external cellular layer of the adventitia of the vessels, the so-called *perithelium*, from which they are supposed to grow.

Angiosarcoma.—An angiosarcoma is any form of sarcoma that contains numerous well-formed blood vessels, about which the cells are arranged. The relation of the blood vessels to the cells of the tissue may be alveolar, tubular, or plexiform. In the alveolar form the blood vessels form plexuses, in whose reticulum the cells cluster, similar to the nests of cells in alveolar sarcoma. In the tubular form the cells surround the blood vessels, as in the *myxangiosarcoma tubulare.* In the plexiform variety the tumor consists chiefly of blood vessels passing in every direction, separated from one another by cells having no definite arrangement. One of the chief characteristics of angiosarcoma is that the blood vessels are better developed than is usually the case in sarcoma, this feature separating the true angiosarcoma from forms which, though rich in blood, are poor in vessels, and are called telangiectatic and cavernous.

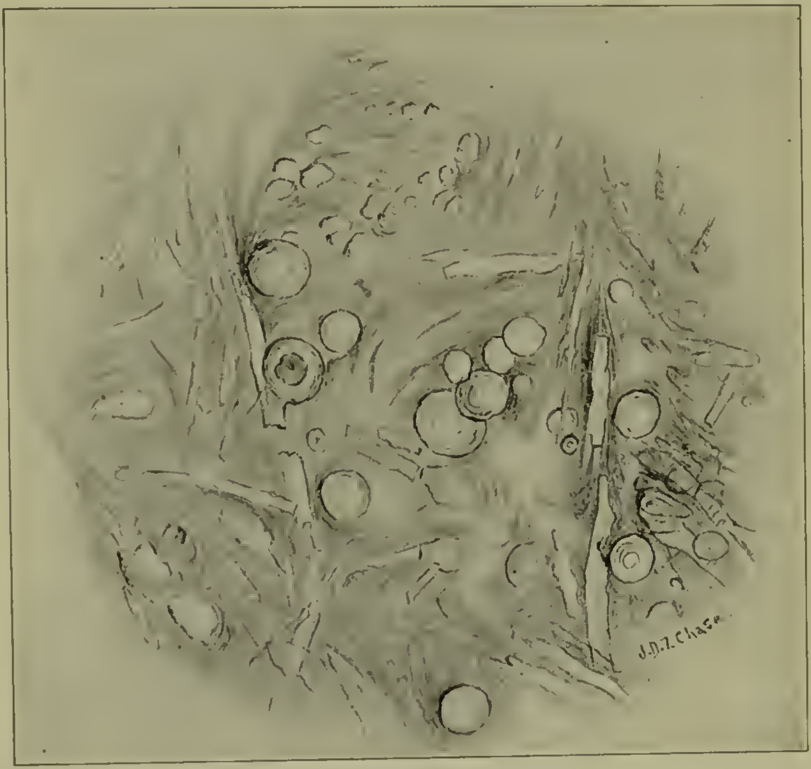

FIG. 86.—Psammoma. The matrix of the tumor consists of a mucous degenerated fibrous tissue in which are numerous spherical and cylindric mineral masses. Oc. 2; ob. 3.

Seat of Occurrence.—Angiosarcoma occurs in the brain, kidney, testicles, lymph glands, skin, and bone.

Morbid Anatomy.—The tumors are dark red or are spotted with red, and not infrequently contain softened areas of interstitial hemorrhage, and on microscopic examination are more or less pigmented with hemosiderin. The cavernous forms contain numerous dilated blood spaces, distinctly circumscribed and lined with endothelial cells.

Psammoma.—The psammoma is usually classified as a form of sarcoma, though sometimes fibrous or myxomatous in character. It is a tumor whose three essential characteristics are a structure rich in spindle cells similar to those of the embryonal connective tissue, hyaline degeneration, and petrification.

Seat of Occurrence.—The tumor is not uncommon in the membranes of the brain and spinal cord.

Morbid Anatomy.—Psammomata are usually small, circumscribed, and granular in appearance. When incised, the knife finds a gritty substance in the tissue. The section is usually rather uniform in appearance, but this will vary with the amount of fibroconnective tissue present.

Pathologic Histology.—Microscopically the tissue consists principally or entirely of spindle cells (psammosarcoma), or of areolar and, sometimes, mucous tissue, or areolar tissue in a condition of mucous degeneration, and always contains a larger or smaller number of rounded, concentrically formed mineral concretions, which are usually identical in appearance with the granules of *acervulin* found in the pineal gland. The concentric mineral bodies are usually small in size and few in number, but may be numerous, and occasionally spicular and cylindric in shape, and in rare cases branched or stellate. Their composition is probably identical with acervulin. The tumors are benign and without clinical importance, except in rare cases, in which they have caused pressure, followed by palsy.

By some the psammoma is regarded as a form of endothelioma, the cells, apparently of spindle shape, being really large flat cells derived from the endothelium of blood vessels.

Osteoid sarcoma develops in the bone marrow and periosteum, and is characterized by the formation of small masses of bone within the tumor tissue. The osteoid sarcoma must be differentiated from the petrifying sarcoma, in which, between columns of cells, spheres and cylinders of lime salts are deposited. The differential feature is that in the one tumor the lime salts are deposited in such a way as histologically to resemble bone, while in the other they are simply mineral concretions. The secondary growths also contain osteoid masses.

Various mixed tumors in which sarcoma cells are associated with simple connective tissues are worthy of brief mention. Among these, chondrosarcoma, which sometimes develops in the parotid glands and other parts of the body in which cartilage is not a normal histologic element, deserves attention. Among the cells of the tumor larger or smaller nests of cartilage, usually of the hyaline variety, can be found. Such tumors are equally prone to undergo myxomatous degeneration, and may thus originate a tumor properly described as myxochondrosarcoma.

II. Composed of Tissues of Adult Type.

FIBROMA.

Fibroma is a tumor composed of fibroconnective tissue of adult type. It occurs in man and the lower animals, and is a common benign tumor.

Seat of Occurrence.—Fibromata are common in the uterus, but are rarely free from considerable admixture of muscular tissue in that situation. They less frequently occur in the ovary and are rare in other organs. The most frequent seat of occurrence is the subcutaneous areolar and intermuscular tissues. They arise from connective tissues, sometimes from the subcutaneous areolar tissue, sometimes from fascia, from periosteum, and bone.

Morbid Anatomy.—Ordinarily they take the form of nodes, which may be flattened when pressed upon by adjacent organs, but may be pedunculated and polypoid when projecting from the surface of the skin. Upon mucous membranes, such as the pharynx or larynx, they almost invariably assume a polypoid form, and may be attached by long, slender pedicles.

The largest fibroid tumors usually consist of fibrous and muscular tissue, as in the myofibroma and fibromyoma so common in the uterus. These may attain the size of a man's head. Of the pure fibromata, the largest perhaps grow from the ovary. In addition to blood vessels, the tumors are supplied with lymph vessels and spaces, and are sparingly supplied with nerves.

The tumors may be small, sometimes not larger than a pin-head, shot, or pea, or may be many pounds in weight. They are usually solid, but may contain colliquation cysts. They may be single or multiple, and are particularly apt to be multiple when occurring in the skin. Fibroma molluscum is characterized by the occurrence of hundreds of scattered subcutaneous nodules. The larger tumors not infrequently seem to consist of amalgamated smaller tumors, appearing on section to grow from several centers. Fibromata are perfectly benign tumors.

Fibroid tumors of the abdomen may, however, attain so large a size and so great a weight as seriously to interfere with the functions of the abdominal organs, and fibroid tumors of the dura mater, by pressing upon the brain substance, may be the cause of palsy or even of death.

The growth of fibroid tumors is usually slow, depending upon the formation and transformation of fibroblasts, ordinary fibroplastic cells, some of which are continually multiplying, while others are transforming themselves into fibers. The rapidity of growth will depend upon the nutrition which the tissue receives, so that vascular tumors in all probability grow more rapidly than others. Clinically it is customary to speak of fibroid tumors as *hard* or *desmoid*, and *soft*. All intermediate forms occur, and the division is without significance..

Pathologic Histology.—The structure of fibroma is extremely simple. It consists of fibers, cells, and elastic fibrils, and differs in no essential from normal fibroconnective tissue. It usually resembles the areolar tissue, but may resemble the denser tissues, such as fasciæ and intermuscular septa. The fibers are arranged in quite regular bundles, which intertwine through the tumor mass in every direction and are apt to form whorls around the blood vessels.

Fibromata are always sharply circumscribed and usually encapsulated. They may be sessile or pedunculated. When a cut surface is examined, they are found to be very compact in structure, grayish or pinkish in color, and fibrous in appearance, the curling bundles of fibers being quite apparent on naked-eye examination. In the majority of cases they are quite well supplied with blood vessels, and may be telangiectatic and pigmented with hemosiderin.

Retrogressive Changes.—Degenerations are of very common occurrence, myxomatous or mucous being most so. The change may occur throughout the whole tumor, transforming what was originally a dense tissue into a soft, juicy one, and causing the tissue to become elastic and even fluctuating in character; or it may be local, with the formation of more or less circumscribed cavities or cysts in the tumor (colliquation cysts).

Fatty metamorphosis very rarely occurs in fibroma. Pigmentation sometimes results from interstitial hemorrhages; these, however, are not very common in tumors of adult connective tissue because of their well-developed blood vessels.

Calcification is frequent, sometimes occurring in the form of diffusely distributed granules of lime salts, sometimes in the form of dense aggregations of mineral matter, which might be correctly described as interstitial calculi, and sometimes deposited in definite lamella identical with bone in histologic structure.

Special Forms of Fibroma.—*Keloid.*—This is a somewhat rare and peculiar fibroid tumor that results from the hyperplasia of a cicatrix, leading to the formation of a mass more or less conforming in shape to the scar from which it grows. Certain individuals are predisposed to growths of this kind, and they are much more common among negroes than among whites.

Keloids usually form projecting elevations with smooth surfaces. They have a pinkish color in Caucasians, though in negroes the skin covering them is pigmented. Rarely they may be irregular, stellate, warty, or otherwise atypical. Scars of all kinds may be succeeded by keloid formations, though they appear to be most common in scars following burns.

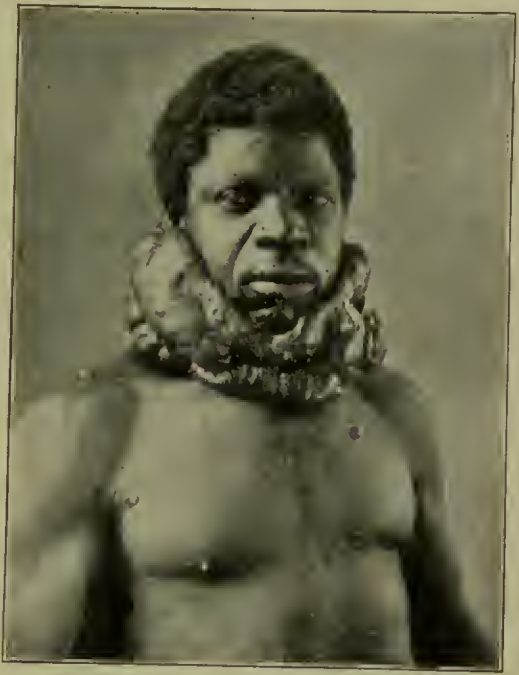

FIG. 87.—Enormous keloids of the neck (Duhring).

Keloids are more frequent in middle life than in childhood. Sutton states that they commonly continue to grow for ten, twenty, or even thirty years, then slowly disappear.

Painful subcutaneous tubercle is a small fibrous tumor, rarely larger than a pea, usually making its appearance upon the surface of the extremities. It is firm, distinctly circumscribed, and movable beneath the skin, and may be so close to the skin as to form a slight prominence, though usually it is first detected by palpation. Upon pressure it is extremely sensitive, and the amount of suffering it may occasion is great, even preventing sleep. Sutton found the tumor more frequent in women than in men. It may appear quite early in life, and in one case he observed one that remained unchanged for eighteen years. It consists of fibroconnective tissue, in which some claim to have found nerve filaments.

False neuroma, a fibrous tumor occurring in the course of nerve trunks and at the ends of amputated nerves (amputation neuroma), will be more fully considered under Neuroma.

Adenofibroma, a mixed fibrous and epithelial tumor common in the mammary gland, will be described under the tumors of that organ.

Molluscum fibrosum, neuromolluscum fibrosum, fibrocellular tumor, dermatolysis, or *pachydermatocele* is a peculiar affection of the skin characterized either by immense hyperplasia of the subcutaneous tissue with hypertrophy of the skin itself, or by the formation of multiple subcutaneous nodes or tumors.

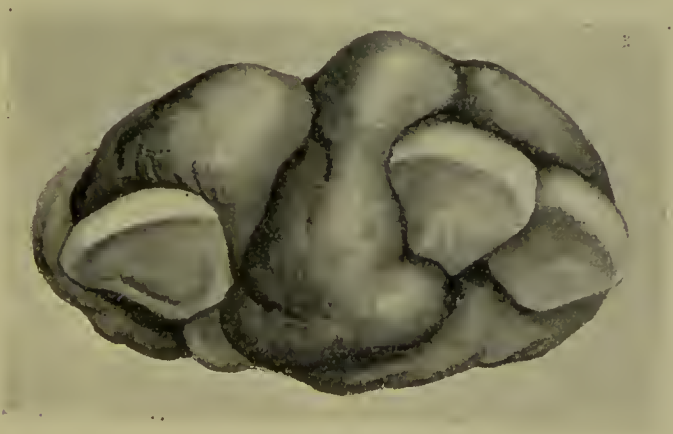

FIG. 88.—Periosteal sarcoma or epulis (Mears)

In cases of the first variety, which involve the scalp, the trunk, or the limbs, extensive areas of the skin become affected and hang in pendulous folds. In the other variety the surface of the entire body may be covered with dozens, hundreds, or even thousands of small polypoid fibrous growths, varying in size from a pin-head to an egg.

The growths are for the most part superficial, though they have been seen in the internal organs, and one is reported to have been attached to the lower part of the spinal column, presumably growing from the receptaculum chyli, and numerous observers have found them growing in the sheaths of the nerves.

Histologically the tumors appear to consist of areolar connective tissue in which nerve fibers are present. Lymphangiectases may occur in the small tumors.

Fibroma molluscum is usually an acquired affection, though in a remarkable case reported by Lamprey, the patient, a native of Sierra Leone, is said to have been born with tumors on the surface of the body.

Epulis.—This is a fibrous tumor arising from the gums or from the periodontal membrane. It usually occurs about the roots of diseased teeth, and may attain the size of a fist, though it rarely becomes larger than a bean. It consists of fibrous tissue covered by the gingival membrane. On account of the presence of the diseased teeth, epuli frequently ulcerate. They do not recur after excision. By Sutton the term epulis is restricted to this form of tumor, though others apply it to various tumors of the jaw.

LIPOMA.

A lipoma is a benign tumor composed of adipose tissue. It is a common tumor that usually makes its appearance in early adult life and subsequently persists. Lipomata are benign. They do no local damage, give no metastasis, and do not recur when excised. In rare cases lipomata growing in the spinal cord have caused transverse myelitis by pressure on the cord. A predisposition to them seems to occur in certain families.

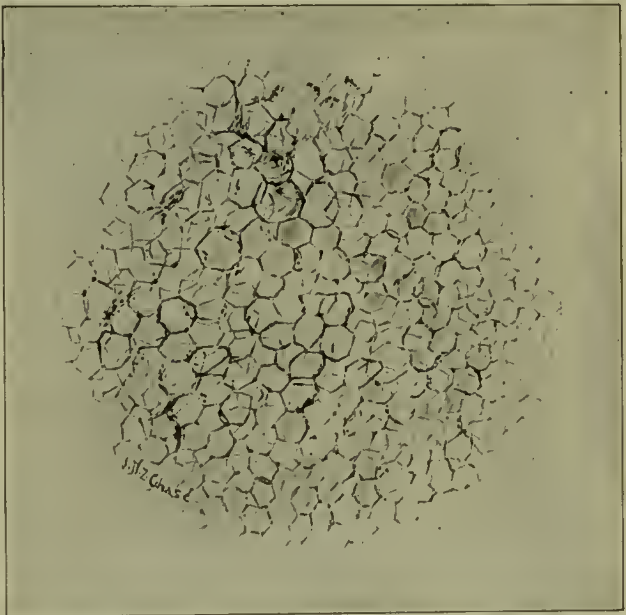

FIG. 89.—Lipoma. The fat cells are polyhedral in shape from neutral pressure. Leitz, Oc. 4; ob. 3.

Lipomata occur in the lower animals as well as in man, and subperitoneal lipomata are not uncommon causes of strangulation in horses. The fats contained in the tumor are those normal to the animal—olein in horses, stearin in cattle, palmitin, stearin, and olein in man.

The tumors may attain an enormous size; the largest known, of which a drawing is preserved in the Warren Anatomic Museum at Boston, is estimated to have weighed no less than 275 pounds, and was attached to a patient who weighed a little over 100 pounds. Lipomata of from 20 to 50 pounds in weight are common. They are frequently multiple, and Broca counted 2080 tumors in one patient.

Seat of Occurrence.—Sutton divides lipomata into eight groups—viz.: 1. Subcutaneous; 2, subserous; 3, subsynovial; 4, submucous; 5, intermuscular; 6, intramuscular; 7, parosteal; and 8, meningeal.

1. **Subcutaneous lipomata** occur in the fatty tissue beneath the integument upon the surface of the body. The fatty tissue of man differs from that of many of the lower animals in that it is distributed over the surface of the body in an equal layer, a little thicker over the trunk and proximal ends of the limbs. The lipomata occur as lobules of this fatty tissue, circumscribed from the rest by their encapsulating connective tissue, so that while in the adipose tissue they are still separated from it. Borden has suggested that the fat forming the lipomata is deposited in certain groups of cells corresponding to those epiblastic cells of the frog, etc., which comprise the fat depots. All authorities agree, however, in believing that the fat in man is stored entirely in the mesoblastic tissues.

Large subcutaneous lipomata may weigh 100 pounds or more. They usually arise from the trunk, shoulders, hips, upper arms, and thighs, but they have been observed upon the face, hands, genital organs, and feet. They are sometimes symmetric, though more frequently so in the diffuse than in the ordinary forms.

2. **Subserous Lipomata.**—These are very apt to form about the hernial openings and about chronically diseased portions of the intestine, such as syphilitic strictures of the colon, etc. They may be small, though some have weighed as much as 53 pounds. Such large tumors usually spring from the omentum. Lipomata occurring about the hernial openings may, by traction or pressure, cause hernia.

Loose fatty bodies are sometimes found in the abdomen, and especially in the sacs of hernia, consisting of detached epiploic appendages. Large pedunculated lipomata of the intestines of horses and cattle are said by Sutton to weigh as much as 2 pounds and be an occasional cause of invagination.

3. **Subsynovial lipomata** arise from the thin layer of fatty tissue beneath the synovial membrane of joints. The most frequent seat of occurrence is beside the patella. The most typical form of this growth is the *lipoma arborescens*, a villous or dendritic fatty growth which seems to be formed by the infiltration of fat into the synovial fringes. It is not infrequently associated with rheumatoid arthritis.

4. **Submucous Lipomata.**—There is but little fat beneath the mucous membranes, so that submucous lipomata are rare. They have been observed projecting upon the inner wall of the stomach, near the pylorus, from the inner wall of the intestine, from the mucous membrane of the larynx, and beneath the conjunctiva. Growths of this form are all small in size. One of the common forms occurs at the external corneoscleral margin, and is known as *pinguecula*.

5. **Intermuscular Lipomata.**—These are not common, though they have been observed between the pectorals, in the tongue, and in the abdominal wall, where they may be very large.

Sutton gives an interesting description of a buccal intermuscular lipoma of symmetric occurrence, which he calls the "*sucking cushion*." It consists of a curious ball of fat, situated between the masseter and buccinator muscles and in close relation to the buccal mucous membrane. It is believed to play an important function in sucking, by distributing atmospheric pressure and preventing the buccinators from being forced between the alveolar arches when a vacuum is created in the mouth, and is relatively larger in infants than in adults. In emaciated children the cushions rarely diminish much in size, though there is scarcely any subcutaneous fat. They sometimes enlarge in adults, especially in cases of impacted salivary calculus in the duct of the parotid gland.

6. **Intramuscular lipomata,** or lipomata occurring in the substance of the muscle, are rare.

7. **Parosteal lipomata** arise from the periosteal membranes. They are usually congenital, and are mixed tumors in which muscular tissue is present. They are very rare.

8. **Meningeal lipomata** occur both inside and outside of the dura mater of the spinal cord. They sometimes contain striped muscular tissue, and are not infrequent upon the sac of *spina bifida*.

Morbid Anatomy.—In most cases a lipoma forms a rounded, lobulated, encapsulated, sessile or pedunculated, soft, elastic, more or less fluctuating tumor. When incised, the yellowish color and fatty texture leave no doubt as to its nature. In nearly all cases the tumor is distinctly circumscribed by a surrounding capsule, in which the fatty tissue seems to be contained under pressure, as when the tumor is incised, the cut surfaces immediately become convex, so that it is impossible again to approximate them. The tumors are very commonly lobulated, and are divided by bands of connective tissue, which may be attached to the integument and cause dimpling of the skin when the tissue is pressed upon. Lipomata are very loosely attached to the tissue matrix, and in consequence are removed by the surgeon with great ease.

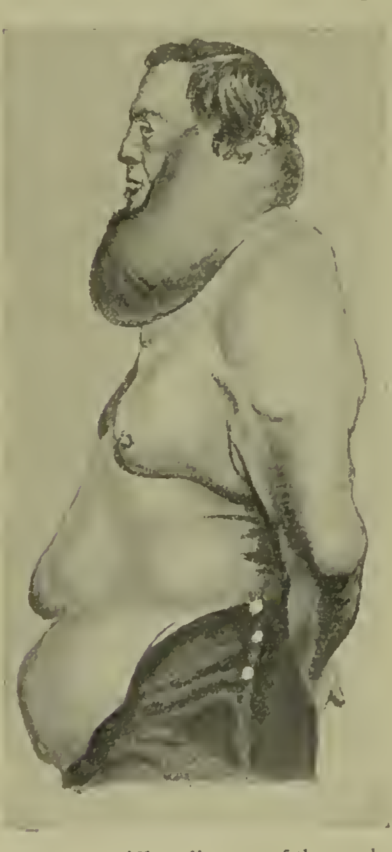
FIG. 90.—Diffuse lipoma of the neck and abdomen (Warren).

The clinical peculiarities of these tumors cause them to be divided into: 1. *Lipoma molle*, a very soft fluctuating tumor with little connective tissue. 2. *Fibrolipoma*, in which there are relatively more connective tissue and numerous fibrous trabeculæ. 3. *Diffuse lipoma*, a badly circumscribed form, not so distinctly encapsulated as the others, occurring usually about the neck, where it often suggests a collar, and if covered with hair, may resemble a fur boa. It is sometimes called *fatty neck*. It also occurs in the axilla and at the groin. 4. *Nevolipoma*, a very vascular tumor, usually of small size, occurring upon the face and subcutaneous tissue, and sometimes springing from the periosteum.

Pathologic Histology.—The minute structure of the lipoma corresponds with that of normal adipose tissue, though the fat cells may be larger and the fibrous trabeculæ more marked. The tumors contain very few blood vessels.

Fatty tissue may occur in combination with sarcoma, myxoma, fibroma, and angioma.

The tumor is subject to few retrogressive changes. The exterior may become inflamed and ulcerate, sometimes causing considerable difficulty in diagnosis, both on macroscopic and on microscopic examination, if too much attention be paid to the ulceration. The septa of lipomata sometimes calcify, sometimes become myxomatous; the fat itself may undergo a change suggestive of saponification.

Lipomata seem to persist after having once formed, and emaciation of the patient has no effect upon them.

MYXOMA.

The myxoma is a benign tumor composed of mucous tissue. It is a rare tumor, whose prototype in the human body is found in the jelly of Wharton of the umbilical cord. Myxomata usually arise as such, but may result from myxomatous degeneration of soft fibromata. It is, however, questionable whether it is correct to speak of tumors of the latter class as myxomata.

Special Forms of Myxoma.—1. *Nasal Polypus.*—This is a pedunculated myxoma which grows from the mucous membrane covering the turbinated bones, from the frontal sinuses or from the antrum. It may be single or multiple, and originates as a sessile node, which soon becomes pedunculated and may later become distinctly lobulated, so that a group of polypi may seem to arise from a common pedicle.

The polypi usually have a smooth covering of mucous membrane and are yellowish or pinkish in color, soft in texture, and are rarely vascular. They sometimes descend in the interior part of the nose, so as to be visible from the anterior nares, or they may descend posteriorly and project through the posterior nares, and have been known to hang down as low as the aryepiglottic fold. They are most common in young adults.

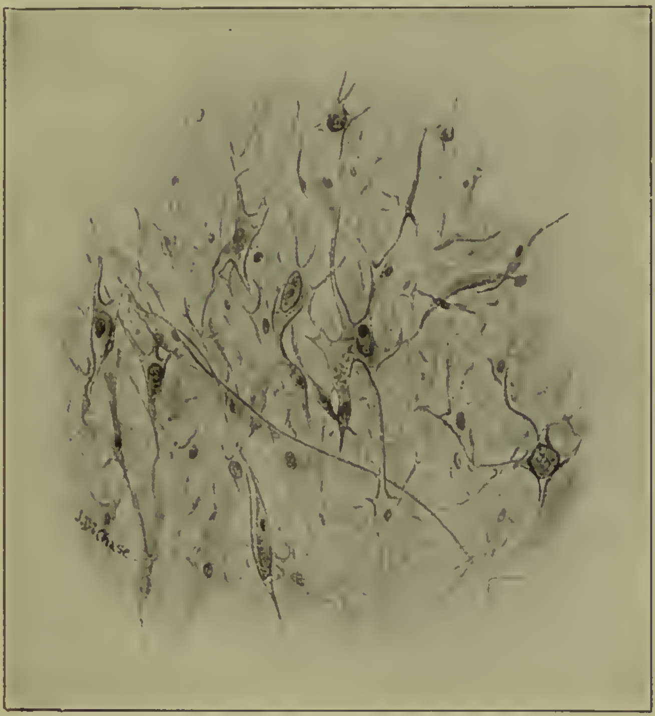

FIG. 91.—Myxoma of the omentum, showing the spider cells of the connective tissue and the meshwork occupied by the mucous substance.

2. *Aural polypi* have their origin in vestiges of a delicate connective tissue that at the time of birth fills the tympanic cavity, but which, as respiration is established, slowly disappears as air from the pharynx works its way up the Eustachian tubes.

Aural polypi usually project externally, blocking up the external auditory meatus and causing deafness by obstruction.

3. *Hydatidiform Mole.*—This peculiar pathologic development is not a tumor, and hence not a form of myxoma. It is the result of a mucous degeneration of the villi of the chorion.

Morbid Anatomy.—Myxomata form more or less rounded, lobulated, circumscribed, and encapsulated soft nodes, which fluctuate, and when incised permit a slimy, mucilaginous or gelatinous material to exude. They may be central, embedded, sessile, or pedunculated. They are benign in nature, but not infrequently recur when removed. Sutton thinks this return is evidence that the tumors in which they occur are sarcomata that have undergone myxomatous degeneration. They do not give metastasis, and generally cause no inconvenience.

Pathologic Histology.—The tissue consists largely of small cells, among which spindle and stellate forms with long anastomosing processes are common. There are also numerous loose fibers, some of which are fine, others coarse and gelatinous. Between the cells and fibers the mucous substance occurs in the form of slime or jelly, and appears in microscopic sections of hardened tissue as a partly granular and partly homogeneous ground substance.

The tumor arises from connective tissue, and most frequently occurs in the subcutaneous, submucous, and subserous tissues, in the fascia, the intermuscular septa, and the periostea. It may also occur in the brain and peripheral nerves and in the interstitial tissue of glands. It is more common in infancy or in early adult life than in the intermediate period or old age.

Myxomata are subject to secondary degenerations, which affect their cells and fibrous trabeculæ. Of these fatty and mucous degenerations are most common.

Hemorrhage, necrosis, and ulceration may occur in myxomata, and sometimes they may become infected and suppurate. Such changes are most frequently observed in tumors predisposed to traumatic injuries, because of their superficial or exposed position, as in nasal polypi.

The softer form of myxoma is sometimes called *myxoma gelatinosum;* the firmer form, *myxoma medullare.*

OSTEOMA.

An osteoma is a tumor composed of osseous tissue. Such tumors usually occur in connection with some part of the skeleton, but are occasionally found in the pia mater, the brain, and the lung. In structure they may resemble the spongy tissue of the epiphyses of the bones, or the dense, ivory-like structure of the petrous portion of the temporal bone, or any intermediate density. They occur in man and the lower animals, and may be solitary or multiple.

Seat of Occurrence.—The most frequent seat of occurrence is the epiphyseal junction of the long bones.

Homologous osteomata—*i. e.*, those resembling the tissue from which they grow—develop upon the inner or outer tables of the skull, the jaws, scapulæ, pelvis, epiphyseal junctions of long bones, and tendinous insertions.

Heterologous osteomata, unlike the tissues from which they grow, develop in the meninges, lungs, diaphragm, parotid gland, and skin.

The bone is formed by metaplasia of newly formed tissue. Cartilage is first formed, then gradually transformed into the bone. Because of this origin, Sutton speaks of them as ossifying chondromata. At times the development of the bony tumor takes place directly from the periosteum, without any intermediate cartilaginous stage. This is described by the Germans as a *connective-tissue exostosis.* A large number of so-called osteomata are not real tumors, but are the result of excessive growth resulting from inflammatory processes. Among these pseudo-osteomata one might mention the bony formations that occur in the muscles of cavalrymen, and depend upon the pressure of the leg against the saddle; or those occurring in the muscles of the arms of soldiers from contact with the musket. Such bony growths are best described by the name *myositis ossificans* (*q. v.*). Also may be mentioned the "spavin" of horses, which is a bony growth resulting from inflammation.

Varieties.—Various forms of osteoma are described. If a new bony growth occurs upon a circumscribed area upon pre-existing bony tissue, it is called an *osteophyte;* if it becomes a distinct, tumor-like, projecting mass, it is spoken of as an *exostosis*. Any irregular bony outgrowth is, however, correctly called an exostosis.

Sutton describes the following forms of exostoses :

1. *Ossification of tendons at their attachments*—resulting from traction, and of which the best examples are the exostoses at the adductor tubercle of the femur and the tubercle of the first rib at the insertion of the scalenus anticus muscle, though the most frequent is that which occurs at the insertion of the tendon of the adductor magnus.
2. *Subungual exostoses*—inflammatory formations of cancellous bony tissue growing from the terminal phalanges and elevating the nail, beneath which they appear like a projecting red cherry, the covering integument usually being ulcerated.
3. *Exostoses due to the calcification of inflammatory exudations*—best illustrated by the peculiar affection known as *myositis ossificans* (*q. v.*).

The greater number of osseous tumors grow directly from the bones, but others are separated from them by periosteum or other intervening tissue, as in the case of *movable periosteal osteoma* and *parosteal osteoma*, which are simply near the bones, and *disconnected osteomata*, which are in the tendons and muscles, etc.

Should such a circumscribed bony formation occur within a bone—that is, within the marrow cavity—it is spoken of as an *endostosis*. A bony tumor that develops from the dentin or the tooth is called a *dental osteoma* (*q. v.*) ; but tumors having a structure similar to the teeth, with dentin, enamel, etc., are spoken of as *odontomata* (*q. v.*). The term odontoma is also employed by many to describe tumors developing from the dental pulp, as well as from the dentin and enamel.

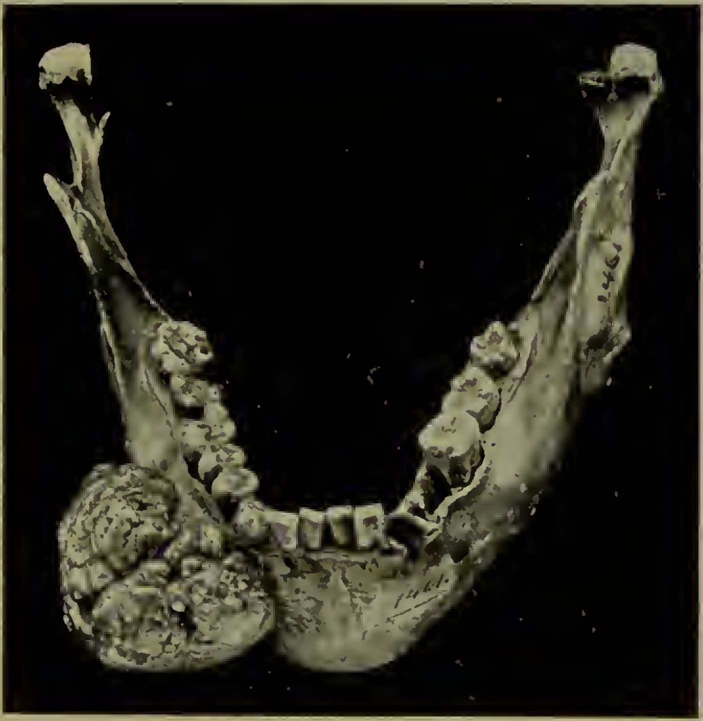

FIG. 92.—Osteoma (Mears).

Compact osteoma, *osteoma durum*, or *osteoma eburneum* is a rare tumor of compact osseous tissue, sometimes of ivory-like hardness, which usually grows upon the surface of the skull and forms projecting rounded masses. It is most frequent in the frontal sinuses, external auditory meatus, and mastoid processes. Osteomata sometimes grow large in the frontal region and extend into the orbit. Sutton speaks of such tumors attaining a weight of 16 pounds in oxen.

Cancellous osteoma, or *osteoma spongiosum* or *medullare*, resembles cancellous osseous tissue with wide marrow cavities. It is usually surrounded by a thick covering of hyaline cartilage. It is common at the epiphyses of the long bones. A diffuse, widespread hypertrophy of bone, by which an individual bone becomes markedly increased in size, is described as a *hyperostosis*.

Bony tumors are benign and do not recur after excision or give metastasis; they grow very slowly. They may be single or multiple in occurrence, and different forms may occur upon the same individual at the same time. They may cause considerable pain when pressing upon the branches of the cranial nerves, and may cause deafness by obstructing the auditory canal. Growth into the skull may also compress the brain.

Morbid Anatomy.—Osteomata vary greatly in appearance according to variety, position, etc. For the most part they form smooth, rounded, more or less lobulated, sessile, hard, bony masses. Sometimes they are irregular and may be pedunculated. They are usually well encapsulated and covered by a thin layer of cartilage.

Osteophytes, such as develop in the membranes of the brain, are thin, translucent plates, conforming to the falx cerebri or other portion of the membrane in which they develop.

The disconnected osteomata of the organs, such as occur in the lungs, appear as branched cylindric formations in the fibroconnective-tissue trabeculæ.

Pathologic Histology.—The structure of the osteoma is typical of bone, though its regularity is less than that of normal bone. Haversian systems can be made out in all, though in the osteoma eburneum they may be few.

Osseous tissue may occur in association with other connective tissues in certain tumors, especially with cartilage, fibroconnective tissue, fatty tissue, and embryonal connective tissue (osteosarcoma).

The most common retrogressive degeneration is mucous metamorphosis, caries and necrosis also occurring. At times the development of a bony tumor is accompanied by a cellular multiplication in the connective tissue, which leads to the formation of an *osteosarcoma*, or a combination of sarcoma and bony tumor. These are more properly considered as sarcomata than as osteomata, and are malignant in disposition.

CHONDROMA.

The chondroma is a tumor composed of cartilaginous tissue, either hyaline or fibrous.

Seat of Occurrence.—The tumors usually grow from the periosteum and medullary substance of the long bones, especially the phalanges of the hands and feet, lower end of the femur, upper end of the humerus and tibia, and more rarely the ribs, pelvis, intermuscular septa, and subcutaneous tissue. Mixed tumors containing cartilage occur in the parotid, submaxillary and lacrimal glands, testicle, and ovary. True chondromata rarely grow from cartilage.

The order of frequency of the tumors that grow from bone is, first, the hands and feet, next, the long bones of the limbs, and lastly, the central portions of the skeleton. Occasionally the cartilaginous tumor commences to grow in the marrow cavity of the bone (*enchondroma*), and distends the shaft of the bone to a barrel shape or spherical form.

The chondroma of the testicle is rarely a pure tumor, but is usually one in which sarcoma and chondroma occur simultaneously—chondrosarcoma—or is a teratoid tumor. Such tumors occasionally take the form of a branched cartilaginous mass, sections of which appear as small nodes and cylinders of cartilage. Occasionally distinct larger nodes are found ; the organ is considerably disturbed by the presence of the masses and by the formation of cysts. The spermatic tubules are not infrequently obstructed and atrophic, and at times contain concentric colloid masses.

Chondromata have also been observed in the ovary and kidney. The chondroma of the lung is usually of metastatic origin, although in rare cases primary tumors of this organ have been found. Chondromata are usually situated at the root of the organ, and probably grow from the cartilages of the bronchi.

Varieties.—The tumors are divided according to the manner of occurrence into the *true chondroma*, *ecchondroma*, and the *enchondroma*.

The *true chondroma* most frequently grows in the long bones, and is most common at the epiphyseal unions, where it seems to develop from unossified remnants of the primitive cartilage. Cartilaginous tumors grow by the vitality of their own cells, which increase in number and produce the intercellular chondrous substance exactly as in the growth of normal cartilages. The tumors are benign in disposition and do not recur when excised, though it is said that they occasionally give metastasis. This is accomplished by the accidental entrance of small masses of the cartilaginous tissue into the veins, this entrance being probably effected by the mechanical erosion of the tissue of the wall of the vein. The cartilaginous embolus which separates is carried to the lungs, in which the secondary tumors occur.

Chondromata are encapsulated tumors, and most common in young persons. They may be multiple and are occasionally very numerous, and cause deep excavations in the bones from which they grow. A few remarkable cases of multiple chondromata of the long bones of the limbs, hands, and feet are on record. They are not infrequent in rickets.

The *ecchondroma* is defined by Sutton as a small overgrowth of cartilage. Ecchondromata are most common along the edges of articular cartilages and in connection with the laryngeal and nasal cartilages. Those of the articular cartilages, especially of the knee-joint, occur in rheumatoid arthritis, while those of the larynx usually spring from the posterior plate of the cricoid cartilage. Ecchondromata of the nasal cartilages are usually small and sessile. The ecchondromata seldom attain large size, usually not being larger than a pea or walnut, and rarely form distinct tumors, but rather simple enlargements or projections from pre-existing cartilage. They are usually of little importance.

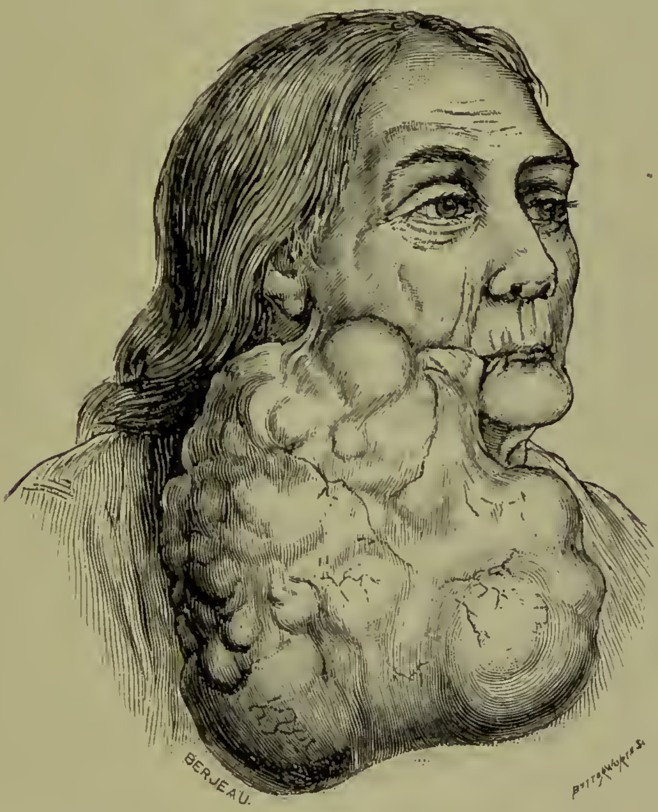

FIG. 93.—Chondroma of the submaxillary gland, which had been slowly growing for forty-four years (Sutton).

An *enchondroma* is a cartilaginous growth which takes place within an organ or tissue; such a growth may appear to be independent of pre-existing cartilage, as, for example, when a tumor occurs within the testicle. Enchondromata are often said to have their origin in injuries to the parts affected. Some of the chondromata probably originate from small masses of primitive cartilage which remain unossified during the development of the bones. Virchow first called attention to this, and demonstrated the existence of such isolated masses of cartilage in the mature bone. It is not difficult to understand that should such a nest of cartilage be excited to growth by traumatic hyperemia, chondroma or ecchondroma might result.

Morbid Anatomy.—The tumors occur as rounded, nodular masses of variable size, which at times become very large, especially when superficial. They are invariably encapsulated by connective tissue (perichondrium), and are divided by intermediate bands of areolar and fibrous tissue, which support the nutrient blood vessels. They are readily recognized by their dense, somewhat elastic structure. Histologically they may consist either of hyalin- or fibrocartilage.

Chondromata are benign in nature, but are sometimes destructive by their size and position, not only interfering with the movements of joints, but causing serious deformity of the members. Thus, small cartilaginous tumors affecting the phalanges may entirely interfere with the movements of the hand.

The chondrosarcoma is different, sometimes being destructive, sometimes showing a disposition to recur after excision, and sometimes causing metastatic distribution. The enchondroma of the parotid gland is said by Virchow to have its origin in remnants of fetal cartilage in the neighborhood of the external ear.

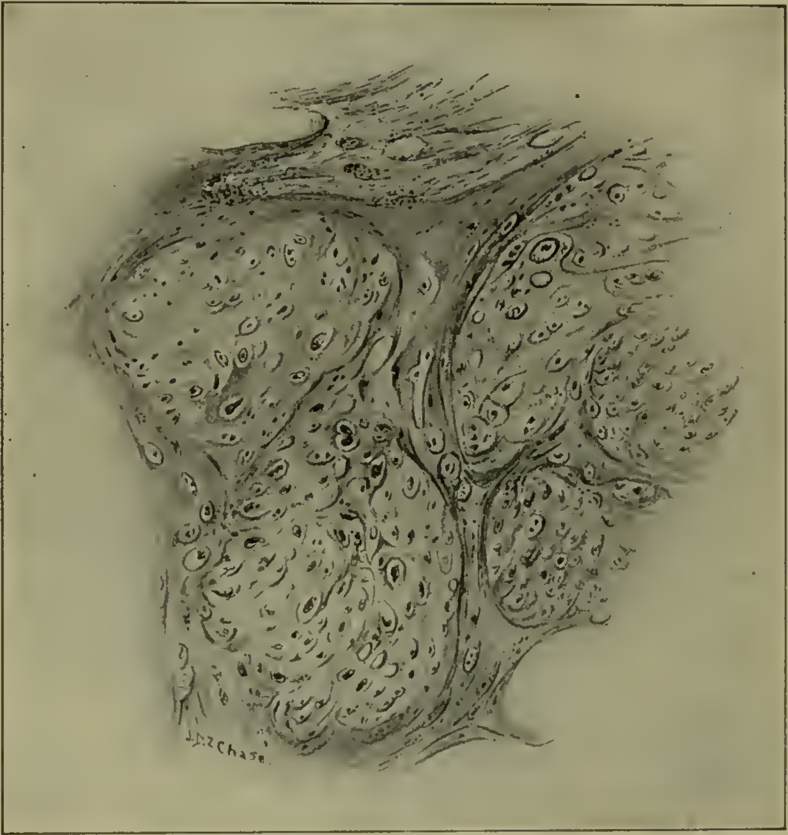

FIG. 94.—Hyaline chondroma. Oc. 2; ob. 3.

Free Cartilages (*Meckel's Cartilages*).—An unusual form of ecchondroma is probably responsible for the occurrence of the free cartilages sometimes observed in the joints, an ordinary ecchondroma, from pressure or other cause, becoming pedunculated, and the peduncle subsequently being compressed between the articular surfaces and becoming more and more atrophic until the little mass becomes free. Such free cartilages interfere with the movements of the joints by occasionally and unexpectedly changing their position, so as to lock the joints. When observed, they may be free or may still be attached by long, delicate pedicles. They may be smooth or worm-eaten in superficial appearance, and are at times calcareous. Sometimes they are symmetric. They are frequent in rheumatoid arthritis.

The tissue of the chondroma frequently undergoes metamorphosis; sometimes the cells contain fat droplets, and the interstitial substance, especially in such tumors as attain to a large size, is apt to undergo mucous degeneration, which may be so complete in its destruction as to cause the formation in the tumors of cysts filled with mucus. Quite frequently calcification of the cartilage occurs, larger or smaller deposits of granules or calcareous masses distributed throughout its substance resembling the centers of ossification in forming bone. True bone is sometimes found, under which circumstance it becomes proper to speak of the tumor as an *osteochondroma.*

MYOMA.

The myoma is a tumor composed of newly formed muscle cells. The muscle cells are usually of the involuntary or unstriped variety, and a tumor so formed is known as a *leiomyoma* or *myoma lævicellulare.* More rarely voluntary or striped muscular tissue occurs in the tumors, which are then known as *rhabdomyoma* or *myoma striocellulare.*

I. **Leiomyoma.**—The leiomyoma is usually composed both of muscular and fibrous tissues.

Seat of Occurrence.—Leiomyomata occur in the uterus, broad ligament, ovary, ovarian ligament, round ligament, and vagina. They also occur in the muscular wall of the intestines, stomach, esophagus, prostate, testicle, and subcutaneous tissue. They usually develop from the unstriped muscular tissue of organs, but in the absence of this they may develop from the muscular tissue of the vascular walls. They occur in man and in the lower animals.

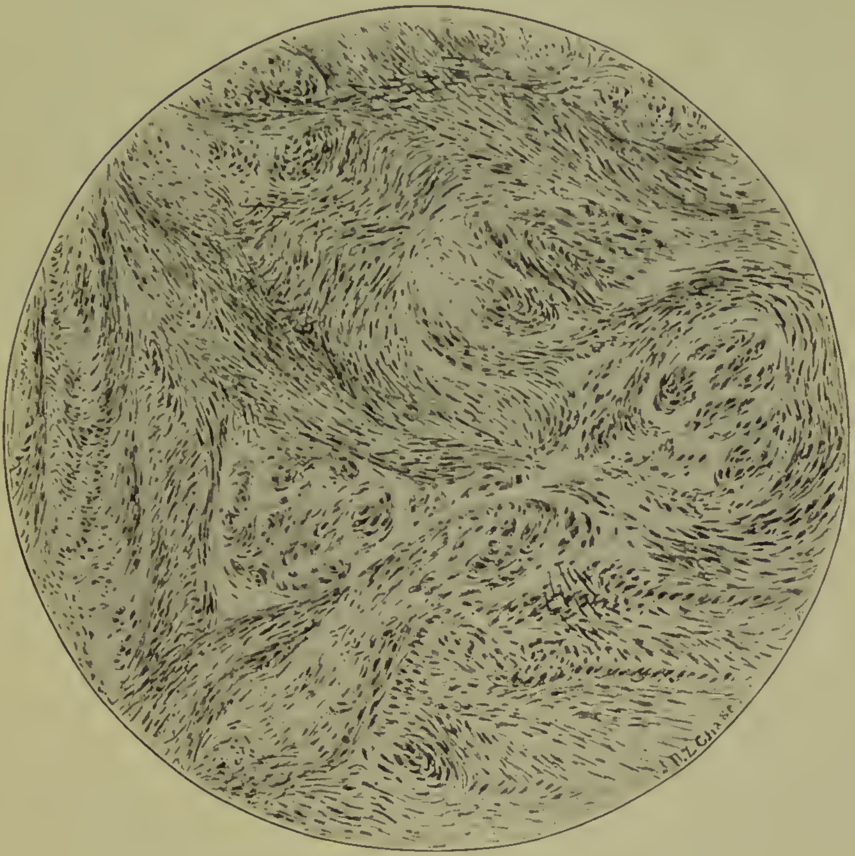

FIG. 95.—Leiomyoma of the uterus (uterine fibroid). Oc. 4; ob. 3.

Morbid Anatomy.—Leiomyomata occur in the form of firm, rounded, nodular, encapsulated masses, which in general closely resemble fibromata, but are usually darker and reddish or gray red in color. The growth is slow, a tumor the size of a child's head probably representing a year's growth. In many cases they seem to attain considerable size, then grow no larger, though persisting for years.

The cut surface of the tumor is almost identical in appearance with that of the fibroma, presenting the same curling, interwoven bundles of fibers. The cut surface is convex.

Pathologic Histology.—Upon microscopic examination the tissue is seen to consist chiefly of elongate spindle cells with rod-shaped nuclei—the familiar unstriped muscle cells.

The spindle cells of myoma are regularly arranged in bundles, their long diameters parallel. The bundles twist, curl, and interlace in all directions, so that in every section of the tumor cells in transverse, oblique, and longitudinal section will be found. The cells can be teased out of the fresh tissue, especially if it be macerated for twenty-four hours in a 20 per cent. solution of nitric acid, or after twenty to thirty minutes' immersion in 30 per cent. solution of potassium hydrate. The longitudinal sections of the cells are best recognized by their rod-shaped nuclei; transverse sections by their polygonal shape. In some cases the spindle cells of sarcoma bear so close a resemblance to the cells of the muscular tissue that it is difficult to differentiate them, but the greater length of the muscle cells, their rod-shaped nuclei, and the polygonal shape of their transverse sections usually serve to differentiate them from the shorter cells of sarcoma, with their vesicular nuclei and more rounded form in transverse section. In most myomata there is a generous admixture of fibroconnective tissue.

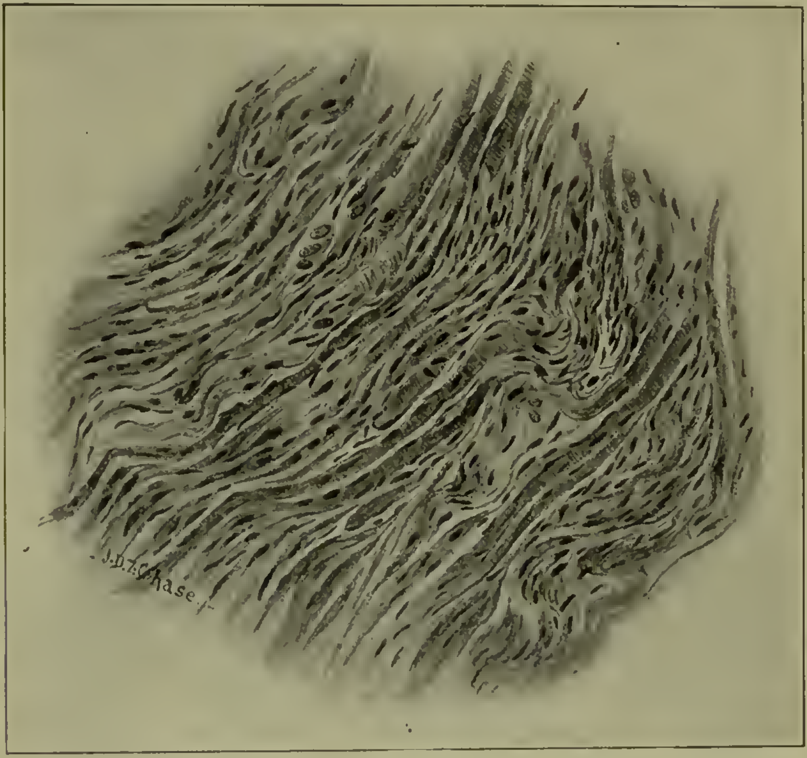

FIG. 96.—Rhabdomyoma. The section shows the tumor to consist chiefly of a fibro-connective tissue rich in cells, with numerous muscular fibers. Oc. 3; ob. D. D.

The tumors are perfectly benign, always being encapsulated and often pedunculated, especially the subperitoneal fibroids of the uterus. They not infrequently cause death from hemorrhage, mechanical pressure upon the bowels, complicating pregnancy or inducing peritonitis by septic necrosis and gangrene. They are subject to degenerative changes, the mucous and calcareous degenerations being common. Sometimes fatty degeneration takes place; necrosis is common; gangrene has been observed. The vessels may become telangiectatic. Hemorrhagic extravasation and the formation of hematomata and colliquation cysts are not infrequent. Ossification sometimes takes place in uterine fibroids.

In some cases the retrogressive degeneration is slow and affects the muscle cells first, leaving the accompanying connective tissue undisturbed, thus transforming the myoma into what appears to be fibrous tissue.

The cysts in myoma form irregular cavities, whose walls consist of softened tissue without sharp circumscription. They always contain mucus. The leiomyoma is often multiple and may be congenital. When in the uterus, it may lead to hemorrhage, dystocia, and sepsis, and when pedunculated, may cause obstruction of the bowels.

II. The **rhabdomyoma** is a rare tumor, Sutton regarding it as a form of spindle-cell sarcoma. It is especially rare as a growth of unstriped muscular tissue. Rhabdomyoma has occasionally been seen in the form of a hyperplasia of muscular structure following traumatic hernia of the muscle, but as a simple tumor formation, it is practically unknown. The occurrence of striped muscular cells among connective-tissue fibers is also rarely observed, and is perhaps doubtfully described as rhabdomyofibroma.

The most usual occurrence of striated muscle is in a peculiar form of congenital tumor of the kidneys in combination with sarcoma cells. The sarcoma cells are usually of spindle form, muscle cells with typical transverse striations being found intermixed with them. The muscle cells usually appear as enormous elongate and nodose striated spindles. The sarcolemma is imperfect. Such tumors are perhaps correctly called *myosarcoma* or *rhabdomyosarcoma*. They may be congenital or develop soon after birth. They attain a large size, are highly malignant, and may give metastasis. They occur in the testicle, uterus, ovary, and parotid gland. In all probability they are teratoid tumors.

GLIOMA.

The glioma is a tumor composed of neuroglia or the connective tissue of the nervous system. Neuroglia is a peculiar specialized tissue, now conceded to be of epiblastic origin. It becomes, therefore, incorrect to classify this tumor among those of the connective tissues of mesoblastic origin, as has been done.

Seat of Occurrence.—Its usual seat of occurrence is the central nervous system—the brain, spinal cord, and retina. Sutton, however, believes the retinal glioma to be a form of sarcoma developing from the sustentacular tissue of the retina.

Morbid Anatomy.—The tumors are usually small, varying in size from a pea to an egg, and are, as a rule, solitary. They are dark red in color and similar to the cerebral cortex in consistence. They may be indistinctly differentiated from the surrounding nervous tissue, and are not encapsulated. Sometimes the tumor is pale gray in color and somewhat translucent. Gliomata are usually quite vascular.

Pathologic Histology.—When examined microscopically, the tissue appears to consist of cells only, these cells being characterized by the presence of nuclei of such large size as to make it difficult to define the delicate cytoplasm about them. When the tissue is properly hardened and stained, it can be seen, however, that the nuclei belong to cells of stellate shape, with many delicate, long, branched processes—typical spider cells. The special staining methods of Weigert and Mallory define the cells well. Among the cells occasional fibers may be seen, the tumors varying somewhat in the number of fibers they contain. As seen in the retina, the tumor consists of cells similar to those of its granular layer. Gliomata are apt to be highly vascular, resembling angiosarcomata, and are liable to interstitial hemorrhage. They not infrequently undergo necrosis and mucous degeneration.

The tumor is benign in disposition, in the sense that it does not recur when completely excised or give metastasis. It is, however, very destructive to the tissue in which it grows, disorganizes it, and invariably returns when incompletely excised. It is easily confounded with sarcoma, and because of the similarity of the two tumors, glioma has come to be regarded with suspicion.

The tumors are of frequent occurrence and are usually solitary. Their growth is slow, and the symptoms produced depend chiefly upon the pressure exerted by the tumor, though in part upon the degeneration of the tissue, as in syringomyelia (*q. v.*). The most frequent seat of occurrence in the brain is the white matter surrounding the ventricles.

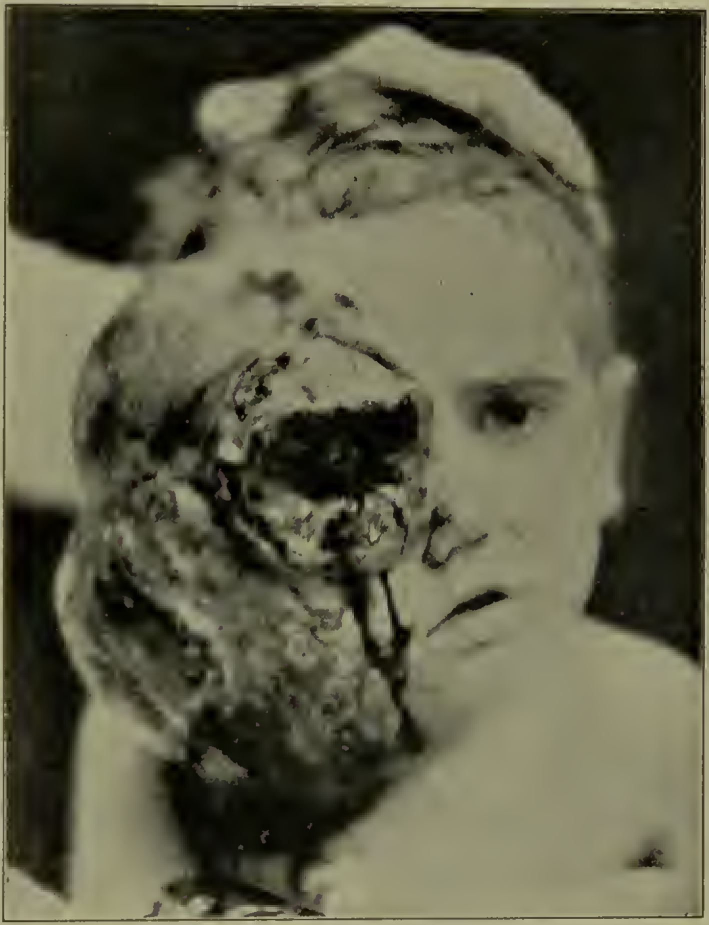

FIG. 97.—Glioma of the retina (from a patient of L. Webster Fox in the Medico-Chirurgical College, Philadelphia).

Warren, who does not distinguish between glioma and sarcoma of the nervous system, states that glioma is the most frequent of all brain tumors. Glioma of the eye frequently recurs after excision, and, having occurred in one eye, after its enucleation sometimes returns in the other. It frequently extends to the cranial cavity from the orbit, and sometimes grows out upon the face, distending the orbit, infiltrating the tissues of the face, and causing great disfigurement.

It is supposed by some that sarcoma and glioma, while different in histogenesis, can be coexistent, and gliosarcoma has been described. This is, however, a very doubtful combination, and in all probability the tumors resembling gliomata, but behaving like sarcomata, are in reality sarcomata.

Glioma is subject to calcareous and myxomatous degeneration and has a pronounced tendency to be hemorrhagic and telangiectatic.

Closely related to the glioma is the so-called *gliosis* of the nervous system, which consists in a diffuse, somewhat nodular, neurogliar hyperplasia, making its appearance near the ventricular and other cavities of the brain and spinal cord. The subsequent retrogressive changes occurring in the hyperplastic tissue lead to the formation of cysts, or when about the central canal of the spinal cord, to its enlargement and the development of *syringomyelia* (*q. v.*).

NEUROMA.

A neuroma is a tumor composed of newly formed nervous tissue. Surgeons apply the term loosely to all tumors occurring upon the nerves, hence it has become necessary to speak of true neuroma, which really consists of nervous tissue, and false neuroma, which is made up of fibroconnective or mucous tissue and occurs upon the nerves.

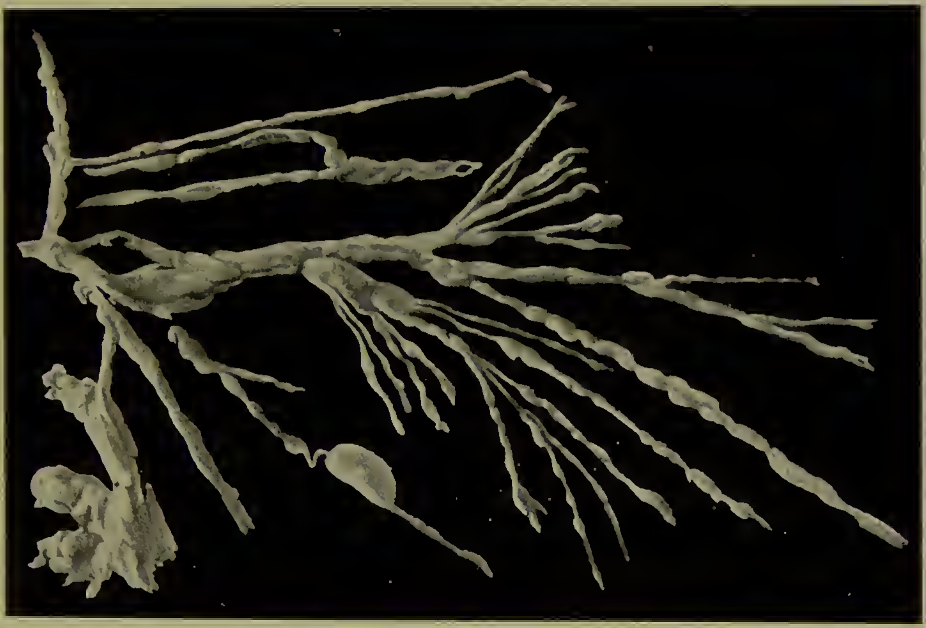

FIG. 98.—Neuromata (Heaton).

It is also necessary to differentiate between *ganglionar neuroma*, composed of nerve cells, and *fibrillar neuroma*, composed of nerve fibers.

I. The **ganglionar neuroma** is a rare tumor which consists of ganglionic nerve cells, neuroglia cells, and nerve fibers, and is usually called *neuroglioma ganglionare*. It occurs in the central nervous system, where it forms ill-defined swellings or circumscribed nodular enlargements. When such enlargements or nodes are incised, the differentiation of white and gray matter seen in normal brains is absent, and the whole area has a pale-gray or mottled gray-and-white appearance. The growth has no sharp circumscription, and it is doubtful whether the formation is properly regarded as a neoplasm or as a malformation. Because of its indefiniteness it may be best to adopt the latter view.

II. **Fibrillar Neuroma.**—Sutton divides these into three forms: 1. Neurofibroma; 2, plexiform neuroma; and 3, traumatic neuroma.

1. The *neurofibroma* includes those forms already mentioned as *false neuroma*, in that they do not grow from the nervous tissue itself, but from the connective tissue of its sheath. They occur on the cerebral and spinal nerves and on the nerve roots, and may be single or multiple. In *neurofibroma molluscum*, which some regard as characterized by tumors of this class, as many as 2000 tumors have been counted.

The neurofibroma is of small size, usually not larger than a lentil or a pea, but may attain the size of the fist. Certain nerves, as the fifth cranial nerve, appear to be predisposed to its occurrence.

It forms smooth, fusiform enlargements upon the nerve, projecting upon one side, and by pressure spreads out its fibers "like a strap." Rarely the fibers of the nerve pass through the center of the growth.

The microscope shows the tumor to consist entirely of connective tissue. Such growths are prone to undergo myxomatous degeneration and may contain colliquation cysts.

The neurofibroma may cause no discomfort, especially if it develop upon a mixed nerve somewhere at the periphery of the body. Upon the sensory nerves, especially the fifth cranial nerve, it may cause very acute suffering. When upon the nerve roots and of considerable size, it may occasion paralysis by pressure upon the cord.

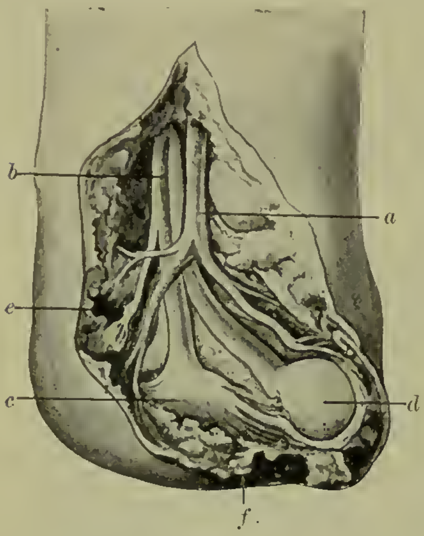

FIG. 99.—Neuromata in a stump after amputation of the foot: *a*, Posterior tibial artery; *b*, posterior tibial nerve; *c*, flat neuroma of internal plantar nerve; *d*, round neuroma of same nerve; *e*, another small neuroma; *f*, cicatrix of stump (Duplay and Reclus).

2. *Plexiform Neuroma.*—This term has been applied by Verneuil to a peculiar and rare condition in which the nerves are increased in number and in length simultaneously with a myxomatous alteration of their sheaths, which transforms them into gelatinous, nodose cylinders, which Sutton has compared to the umbilical cord. The term *cirsoid neuroma* has also been applied to the condition.

The growth makes its appearance upon the head, trunk, and extremities, where the skin becomes thickened and loose, so as to bear a partial resemblance to elephantiasis. When the tumor is pressed beneath the fingers, the enlarged nerves can be felt like worms in a bag.

The tumors are usually congenital. When subjected to microscopic examination, it is found that the nerves have undergone a fibrosis from excessive growth of the endoneurium, which is thickened and nodose. The myxomatous degeneration occurs in this hyperplastic tissue.

Both medullated and non-medullated nerves have been found in plexiform neuroma, though the former predominate.

3. *Traumatic or Amputation Neuroma.*—These are bulb-like growths which form upon the proximal ends of divided nerves or upon the cut nerves in an amputation stump. Their growth seems to depend upon attempted regeneration of the nerve, whose axis-cylinders grow down into the cicatrix and spread out. Later the connective tissue also grows down and ensheaths them, and many of the fibers become medullated. The bulbous ends which thus form on the nerves may be the size of a pea or of a pigeon's egg. They are smooth, not sharply differentiated from the surrounding tissue, and are firm to the touch. The microscope reveals their true nature.

They cause great suffering in some cases, though in the majority of instances they are painless and not sensitive to pressure.

All forms of neuroma are benign. They may, however, necessitate operation because of pain and deformity. The greater number are congenital, and a distinct hereditary tendency to their development seems to be present in some cases.

They are not common in the lower animals, though the amputation neuroma is frequently seen upon the limbs of animals injured in traps, by gunshot or bites, and they not infrequently form on the divided nerves of horses after the operation of neurotomy.

Malignant neuroma, which has occasionally been described, is in all probability a sarcoma of the nerve sheath and not a tumor of the nerve.

ANGIOMA.

An angioma or hemangioma is a tumor consisting essentially of blood vessels, some of which are of new formation.

The **etiology** of the tumor is obscure. Some forms seem to depend upon an abnormal dilatation of the blood vessels belonging to the tissue in which they occur; others upon dilatation of these vessels associated with the formation of new ones. In most cases the growth is entirely without distinct boundaries, and presents radiating extensions, as are observed in *nævus araneus* or "spider cancer" of the face. Sometimes, as in the *plexiform angioma*, the dilated vessels are cirsoid and parallel, the dilatation and tortuousness extending some distance beyond the confines of the tumor along its supplying vessels. In other cases, as in the cavernous angioma of the liver, the growths are quite well defined.

Angiomata occur in the skin and subcutaneous tissue; the subcutaneous and subserous tissue; in the muscles and bones, and in certain organs, especially the liver, kidneys, spleen, intestine, and bladder.

In the subcutaneous tissue it is often difficult to differentiate between phlebectasia (*q. v.*) and angioma, though limitations of the vascular dilatations might be a safe guide to follow.

Special Forms.—1. Angioma simplex or **simple nevus,** also called *angioma glomeruliforme, angioma telangiectasia, nævus vascularis,* or "birth mark," is the most frequent and simple form. It consists of capillaries, small arteries, and veins, which are woven together into a complicated reticulum or plexus of vessels that may show saccular dilatations when microscopically examined.

These tumors are most frequent in the skin, where they are frequently observed at birth, and are in consequence known as "mother's marks" or "birth-marks." They may be observed at the time of birth or appear a few weeks later. They may remain inconspicuous in size, but sometimes a very trivial mark, deserving of no attention in infancy, may grow to considerable dimensions and even prove dangerous in after-life.

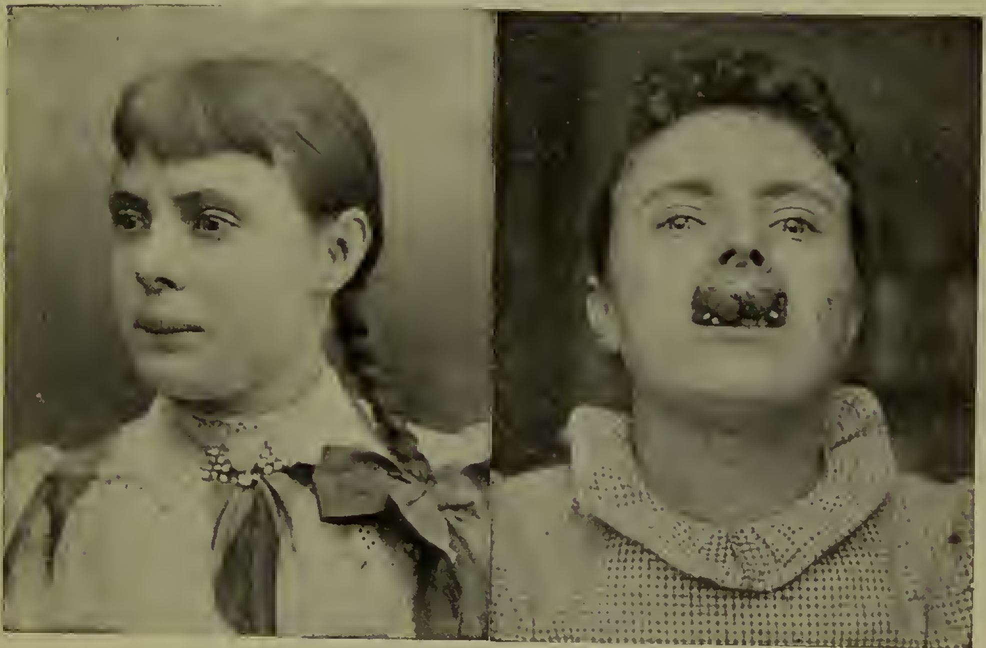

FIG. 100.—Angioma of upper lip (Dandridge).

The superficial or dermal nevi appear as discolorations rather than as enlargements or elevations upon the skin, though in exceptional cases distinct and fairly well circumscribed tumors occur. They are apt to occur near one of the points of fusion of embryonal tissue (fissural angioma).

A nevus may appear brilliant red in color (*nævus flammeus*), or reddish purple or bluish purple (*nævus vinosus* or "port-wine stain"). These discolorations may form mere points upon the skin, or may cover an area of one or two square centimeters. They often present fantastic shapes, which has suggested a correspondence between the spots and objects that profoundly impressed the parent before the birth of the child. While fortunately small, as a rule, nevi of this class may spread over half of the face, or in exceptional cases over a large part of the body. The skin covering them is usually smooth, but may be coarse and granular. *Nævi pigmentosi* or pigmented moles are more complicated in structure and may be covered with fine hairs.

The simple nevi occur chiefly upon the face, but may also occur upon the scalp, neck, back, labia, genitalia, lips, tongue, and conjunctiva, and rarely in the membranes of the brain and spinal cord. Simple angiomata also occur in the mammary glands, in the bones, and occasionally in the brain. Certain of the vascular polypi commonly included among the *hemor-*

rhoids (*q. v.*) are simple angiomata resulting from dilatation of groups of minute arterial or venous vessels. They are usually situated within the sphincter muscle of the anus, forming *internal hemorrhoids* of pedunculated form and sometimes of berry-like appearance. Dilatations of small arteries and their distribution occurring in this way are sometimes described as *racemose aneurysms*.

Pressure upon a nevus drives the blood from the vessels, causing it to pale, the pallor immediately disappearing when the pressure is removed. If the growth is thicker than usual and forms a flat, tubular, or warty swelling, and especially if it contains an unusual number of arterial vessels, it may pulsate. Such distinct enlargements sometimes show thickened capillary walls (*simple hypertrophic angioma*). If a port-wine stain contains unusually large vessels, it is sometimes called *angioma simplex venosum* or *varicosum*. In the vessels of such tumors small phleboliths (*q. v.*) may form.

Simple angiomata may remain unchanged throughout life; in rare cases they spontaneously disappear. Unfortunately, the growths sometimes take on an unexpected development and become transformed to *cavernous angiomata*.

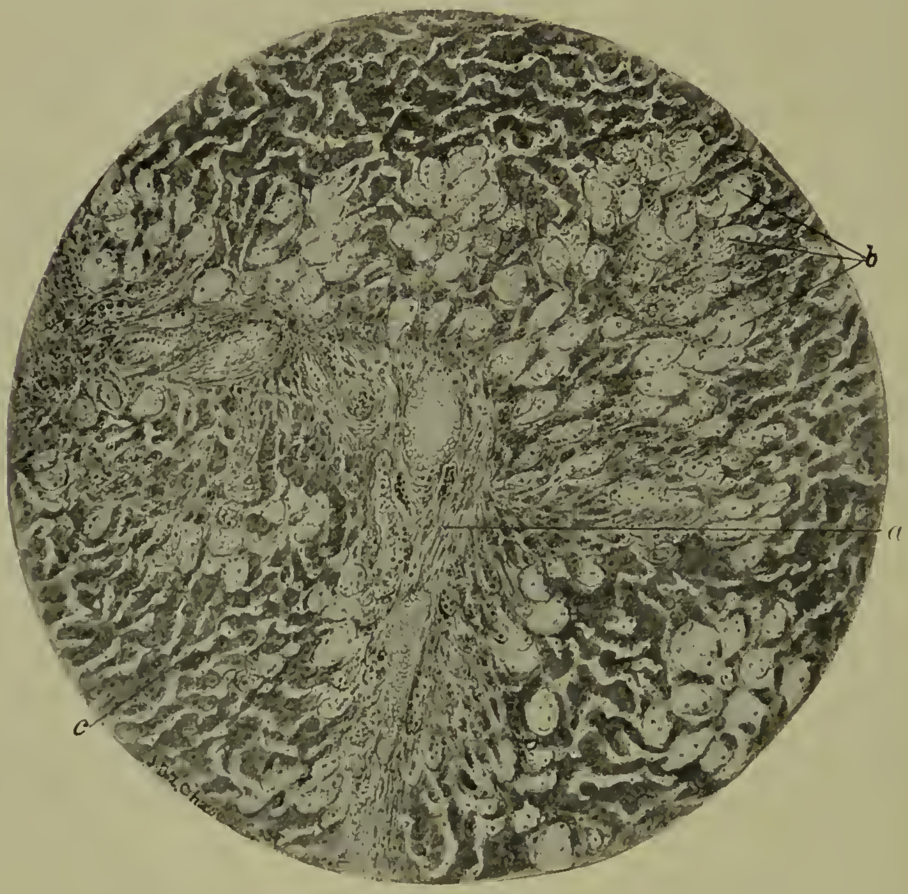

FIG. 101.—Racemose angioma of liver: *a*, Periportal connective tissue containing a vein and bile-ducts; *b*, dilated capillaries forming tumor; *c*, liver cells.

When a simple angioma is examined with the microscope, the vascular dilatations are found to be cylindric, fusiform, and saccular, the vessels freely communicating with one another.

2. **Cavernous Angioma or Angioma Cavernosum.**—In this group are included vascular tumors whose structure approximates that of the erectile tissue, consisting of widely dilated, irregular blood cavities, separated from one another by connective-tissue partitions. The cavities thus formed freely communicate with one another and are all lined with endothelium.

The angioma cavernosa occurs in the skin and subcutaneous tissues, and is formed either by dilatation and consequent transformation of simple angiomata or by the new formation and progressive dilatation of ordinary vessels. Angioma cavernosa also occurs in the mamma, tongue, bones, voluntary muscles, larynx, kidneys, spleen, uterus, intestine, and bladder.

The dermal growths present a color similar to that of the simple angioma, appearing pink, red, purple, or blue. They are larger than the simple angiomata, and form more or less prominent tumors, some of which become as large as goose eggs and frequently pulsate distinctly. For the most part they form ill-defined swellings or nodes, though in the larynx they may

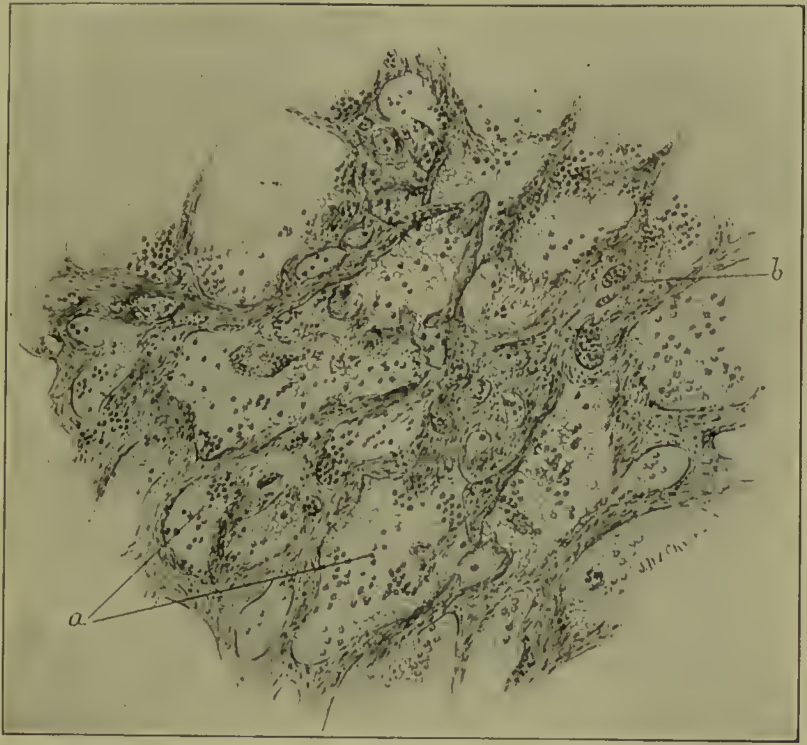

FIG. 102.—Cavernous angioma of liver. The illustration shows tumor tissue only: *a*, Blood channels filled with corpuscles; *b*, fibrous framework supporting delicate walls of blood sinuses.

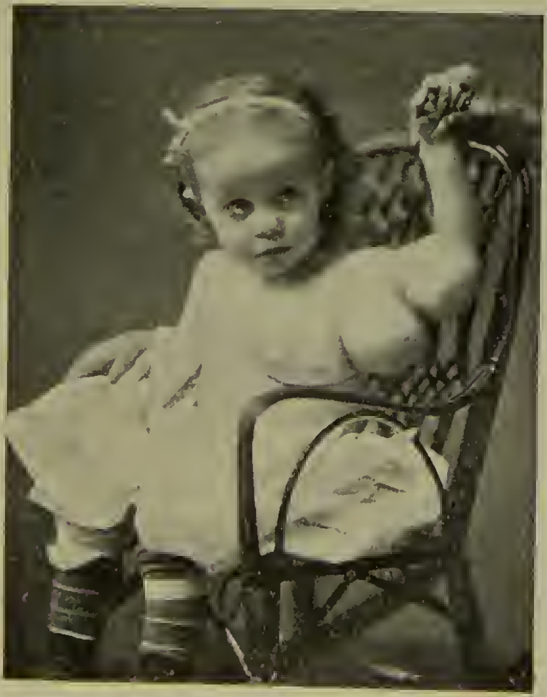

FIG. 103.—Cavernous lymphangioma of the axilla, of congenital origin (Warren).

take the appearance of sessile or pedunculated tumors (*nævi prominens*). They may be diffuse, or may be fairly well circumscribed and even encapsulated. They have a peculiar spongy character and readily yield to compression, the blood being driven into neighboring vessels.

Cavernous angiomata are common in the liver, where they appear as dark spots which collapse after death and appear somewhat depressed upon the surface. The hepatic angiomata are often multiple, especially in aged persons, and are believed to be acquired late in life.

Cavernous angioma is less benign than simple angioma, its progressive enlargement compressing the tissue in which it grows, causing its atrophy. The attenuation of the walls of the dilating vessels predisposes to rupture with frequent hemorrhages, which may result in anemia or even be fatal.

3. **Plexiform angioma, cirsoid aneurysm, aneurysm by anastomosis, angioma arteriale plexiforme,** or **angioma arteriale racemosum** is a rare abnormal growth in which an entire group of arteries becomes dilated, tortuous, irregular, and hypertrophied, and forms a vascular mass in which the vessels, for the most part, are nearly parallel. Arteries of middle size are so affected. It forms a tumor-like enlargement, but might with equal propriety be described as a congeries of cirsoid aneurysms.

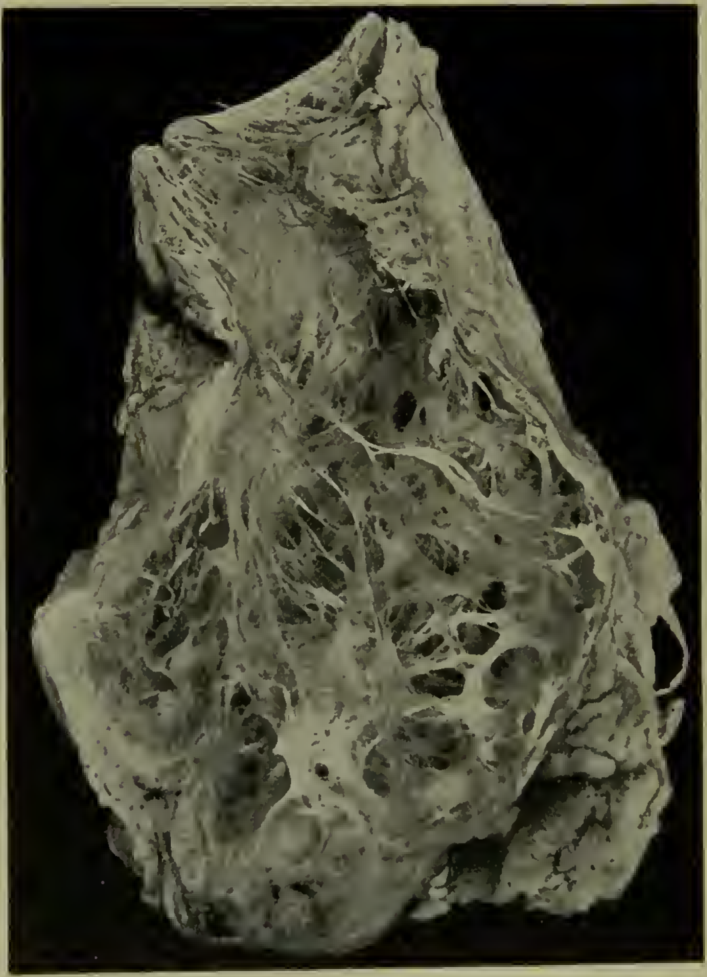

FIG. 104.—Cavernous lymphangioma of neck and axilla in a young woman (Homans).

Sutton says that plexiform angiomata may consist of arteries only, of veins, or of arteries and veins in equal proportion.

Plexiform angiomata have been observed upon the face and head, upon the perineum, forearm, and in the popliteal space. A distinct bruit or "buzz" has been subjectively detected in the cases in which the tumor occurred upon the head.

Morbid Anatomy.—Angiomata are made up of arteries, veins, capillaries, and lymphatics, with intervening tissue corresponding to the structure in which they form. The differentiation of arterial from venous vessels may be difficult when the dilatations are considerable and numerous, and impossible if the arterial and venous channels communicate. Capillaries may be absent. In the cavernous angioma it is impossible to recognize the origin of the blood spaces, which are simple, wide channels through which mixed blood circulates.

Pathologic Histology.—The microscopic examination reveals nothing more than can be recognized by the naked eye. The tumor is found to be composed of atypical and, often, attenuated blood vessels of all varieties.

LYMPHANGIOMA.

The lymphangioma is a rare tumor, essentially composed of lymphatic vessels. This tumor bears the same relation to the lymphatic vessels that the hemangioma does to the blood vessels. It consists of a simple dilatation of groups of lymphatic vessels (*lymphangioma simplex*), usually affecting their whole length. Sometimes large saccular dilatations are formed, and the growth is called *lymphangioma cavernosum* or *cystoides*. The fluid contents of these cysts is commonly milky in appearance.

No distinct tumor is formed, but the dilated vessels may alter the shape of the affected part or lead to universal increase in its size. Thus, *macroglossia*, *macrocheilia*, and *nævus lymphaticus* are respectively characterized by lymphatic dilatation of the tongue, lips, and local areas of the skin. The condition may be congenital or acquired; its cause is unknown. In rare cases obstruction of the lymphatics with enlargements similar to those described result from parasitism, and the disease known as *elephantiasis* (*q. v.*), which is characterized by marked lymphangiectasis, is known to have its origin in obstruction of the lymphatic vessels by filarial worms.

Rarely the thin dermal covering of the lymphangiomatous enlargements gradually atrophies, and should the cysts or the dilated vessels rupture, a permanent fistula remains, leading to lymphorrhea.

Chylangioma resulting from dilatation of groups of lacteal vessels is rare.

LYMPHADENOMA.

There are few pathologic lesions concerning the nature of which we are in such uncertainty as the lymphadenoma.

From the surgeons, many of whom were pioneers in the description of pathologic processes, we have had handed down to us the word *lymphoma*, which was applied indiscriminately to all enlargements of the lymphatic nodes, so that tuberculosis, simple infection, hypertrophy, and neoplasm were all included in its scope. We even read of *hard* and *soft lymphomata*, these words referring merely to the physical condition of the affected nodes, and not enabling one to make any important differentiation of the lesions. The term lymphoma should, therefore, be abandoned. When we eliminate the hypertrophies, hyperplasiæ, infections, and other lesions of the nodes, there remains an enlargement not yet accounted for and described as lymphadenoma.

A *lymphadenoma* is a tumor formed by proliferation of lymphoid tissue, and usually develops from lymphatic nodes.

It is doubtful whether the latitude permitted by this definition is not too wide, as it is not known whether all such growths arise from the same cause, as we have no positive knowledge of the nature of any of them.

There is a widespread opinion in the profession that the so-called lymphadenomata are not neoplasms, but lesions of some not yet understood specific infection.

Multiple lymphadenoma is variously known as Hodgkin's disease by Wilks, who so named it after Hodgkin, who first described it in 1832; as pseudoleukemia by Cohnheim; adenie by Trousseau; lymphadenie by Ranvier; malignant lymphoma by Billroth; lymphosarcoma by Virchow; malignant lymphosarcoma by Langhans; and lymphadenoma by Wunderlich and also by Ranvier.

The enlargement is characterized by proliferation of the lymphoid tissues, chiefly of the lymph nodes. One node may be affected, though more frequently a chain of glands enlarges either simultaneously or in succession. Lymph nodes over all the body, and lymphatic tissue in all the organs, may show proliferation and enlargement (general lymphadenoma). Such cases would closely resemble leukemia, but the blood changes of that disease are not observed, the only blood changes present in lymphadenoma being secondary anemia resulting from the occasional cachexia. The successive enlargement of lymph nodes of the same region makes it difficult to differentiate between lymphadenoma and tuberculosis of the lymphatic glands, and it may be impossible properly to differentiate the two conditions clinically.

The growths may be as large as horse-chestnuts, or in exaggerated cases as large as eggs. The consistence of the nodes is altered, and they become soft, at times even fluctuating; the cut surface is white and not unlike the white matter of the brain. From this change in appearance it must be concluded that the growth is more than either a hyperplasia or hypertrophy. The lymphoid structure of the organs is also distinctly changed. Thus, the tonsils hypertrophy and their follicles become greatly enlarged. The spleen is not uniformly enlarged when affected, but contains nodules of lymphoid tissue.

Pathologic Histology.—The enlargement of the lymphoid organs depends upon increase in the number of lymphocytes, chiefly the small lymphocyte normal to the lymphatic tissue, though some multinuclear and endothelial cells can usually be detected in the growths. The lymphadenoid structure—*i. e.*, the delicate reticulum with aggregations of lymphocytes in its meshes—is usually retained; the relation of lymph sinuses, cortical follicles, and medullary cords is, however, destroyed.

The tumors once having formed, usually persist. They may occur at any part of the body, but seem to be most frequent in the neck and mediastinum. Though they become very soft, they rarely break down and discharge the contents, or by rupture of the capsule permit infiltration of the neighboring tissues.

The tumor cannot be called benign, because it is apt to be followed by anemia and cachexia, and because some of the tumors tend to malignant infiltration. Many cases clinically diagnosticated as lymphadenoma, especially when of the infiltrating variety, prove upon careful microscopic examination to be tuberculosis of the nodes.

Lymphosarcoma is too closely related to the tumor just described to receive separate consideration. It has, however, certain characteristics by which many cases can be differentiated. That is to say, though it arises from the lymphoid tissues of the lymphatic nodes, spleen, and tonsils, and from the lymph follicles of the pharynx, palate, stomach, and intestine, and retains the lymphoid structure fairly well, it early breaks through the surrounding capsule, invades the adjacent tissues, and establishes secondary growths by lymphatic or hematic metastasis. Superficial growths of this kind, such as occur in the intestine, pharynx, etc., early undergo necrosis, with the formation of large ulcers. By the fusion of neighboring masses conglomerate tumors may also be formed.

From this brief description it will become apparent to the reader that the difference between lymphadenoma and lymphosarcoma is very slight. Both may be infectious lesions, not neoplasms, and both may depend upon the same cause.

TUMORS OF THE EPITHELIAL TISSUES.

The tumors of the group next to be considered are characterized by component tissues derived from two of the blastodermic layers—the epiblast or hypoblast and the mesoblast. Epithelial cells, though not always present in large numbers, form their essential and conspicuous elements. Because of the importance of the epithelium which they contain these tumors are commonly described as *epithelial tumors*. Because of their composite nature and more or less pronounced resemblance to organs Virchow called them *organoid tumors*.

They all consist of a vascular fibroconnective-tissue framework, in or upon which the epithelial cells are situated. The relation of the two tissues varies according to the type of tissue from which the growths arise; thus, under normal conditions, the surfaces of the body are covered with a layer of epithelial cells supported and vascularized by a subepithelial tissue characterized by papillæ which carry the capillary vessels and nerve endings and afford additional surface for the attachment of the epithelium. The tumors of this tissue either consist of exaggerations of the normal structure—that is, enlargement of the papillæ, about which, as a central axis, the increased epithelium is developed (papilloma)—or are due to a loss of the proper relationship between the epithelium and the subepithelial tissue, by which the former grows down into and invades the latter (epithelioma). The greatest difference in the disposition of the growth arises in consequence of its mode of origin, for a tumor of the first form becomes merely a harmless excrescence, while one of the last form becomes an invading, disorganizing, recurring, and metastatic tumor.

The other epithelial structures of the body are collectively considered as "glands," and consist of a vascular and fibrous reticulum whose spaces contain the essential functional cells. Tumors which maintain this structure and show a normal relationship between the epithelium and connective tissue are as harmless as the normal tissues; but if once this relationship is destroyed and the cells are no longer held in bounds by the membrana propria, but find themselves at liberty to multiply in and extend along the interstices of the connective tissue, the growth becomes entirely different, and results in disorganization of the affected organ with a tendency to metastatic distribution.

It is, therefore, by consideration of the order or disorder shown in the structure of the tumor that its disposition as regards malignancy or benignancy can be judged. Normally, the epithelial cells are arranged in an orderly manner upon a membrana propria, which forms a sharp line of demarkation from the adjacent connective tissue. The line of the membrana propria is rendered irregular by minute outgrowths of the connective tissue (papillæ) and by tabular ingrowths of epithelium (glands). Tumors formed by an atypical new formation of papillæ or of glands, the orderly relationship of the cells to the membrana propria being preserved, are called respectively papillomata and adenomata. Tumors resulting from an atypical, unlimited, infiltrative overgrowth of epithelium, the orderly arrangement being lost, with the result of invasion of the connective tissue by the epithelium, are called *carcinomata* or *cancers*.

The term *epithelioma* is sometimes used in a broad sense to refer to whole groups of the epithelial tumors, but it has become customary to restrict this term to a certain form of superficial cancer.

PAPILLOMA.

A papilloma is a benign tumor resulting from a new growth of epithelial-covered papillary processes arising from the skin or mucous membranes.

Seat of Occurrence.—Papillomata are common upon the skin and also upon the mucous membrane of the larynx, nose, and bladder. They sometimes also occur in cysts of the ovary and mammary gland and in cysts of certain tumors (papilliferous cysts—adenocystoma papilliferum).

They occur in man and in the lower animals, being frequent upon the penes of horses and bulls, lips of lambs, and pads of the feet of carnivorous animals.

Morbid Anatomy.—The appearance will vary according to the variety. It is customary to divide the tumors into *hard papilloma*, which occurs upon the skin and consists of papillary processes covered with squamous epithelium, and *soft papilloma*, in which the papillæ are covered with columnar epithelium. Sutton gives a different classification, dividing the tumors into: (1) Wart; (2) villous papilloma; (3) intracystic papilloma, and (4) psammoma.

The psammoma is now generally conceded to originate from endothelium, not epithelium, and is, therefore, more closely related to the sarcomata, with which it is described in this work.

The "warts" are hard papillomata; the villous papillomata, either hard or soft, according to the tissues from which they arise; all the intracystic papillomata are soft.

1. **Hard Papilloma, Verruca, or Wart.**—These dermal neoplasms are common upon the hands of children (verruca vulgaris), where they form small single or multiple sessile growths, rarely much larger than a pea. They frequently appear in successive crops, growing in a surprisingly short time, and often disappearing with equal celerity; sometimes they persist. The little growths are irregular and hard, and through attrition of the superficial epithelium frequently show, upon the partially denuded surface, the numerous papillæ forming the foundation of the structure. Such warts are sometimes popularly known as "seed warts," probably under the misapprehension that the little papillæ are seeds. Softer warts are of frequent occurrence about the anus, and especially upon the glans penis and vaginal wall as the result of the irritation of gonorrheal discharges, etc. These are known as *verruca acuminata*, *condylomata acuminata*, or *venereal warts*. They are more polypoid than the ordinary warts, and are softer and more red, being much more vascular. A warty outgrowth situated chiefly about the genitals, though occurring upon other moist dermal areas and upon the squamous mucous membranes in syphilis, is known as the *condyloma lata*. It fails to present the usual warty appearance because of the rapid degeneration of the superficial cells, so that it forms a flat, glazed, semi-ulcerated area, familiarly known as the "mucous patch."

Rarer forms of warts are the *verrucæ digitata*, consisting of numerous long, projecting, finger-like processes, which appear upon the scalp, shoulders, and back; and the *verrucæ filiformis*, elongate, thread-like growths upon the face and neck.

Many warts persist and increase in size, and may even attain a size as large as the fist, and, as Sutton says, "look very formidable." The surface is not infrequently necrotic in the larger tumors, and the discharge from it may be very offensive.

The spontaneous disappearance of warts is dependent upon loss of nourishment, followed by softening and exfoliation of the growth.

Laryngeal warts usually spring from the mucous membrane covering the true vocal cords, near the point of attachment to the thyroid cartilage. They frequently resemble a mulberry, and by being nipped between the cords, may obstruct the glottis and cause suffocation. They rarely attain a size larger than a cherry, and the greater number are not larger than pin-heads.

2. **Villous papilloma** may occur upon mucous membranes covered with squamous cells, or upon membranes covered with columnar cells.

(*a*) *Squamous-cell villous papilloma* is not infrequent in the urinary bladder, where it forms a delicately branched dendritic growth, most apt to spring from the posterior wall of the bladder, near the trigone. They also grow occasionally in the pelvis of the kidney, and when they occur simultaneously in both situations, it is not impossible that a fragment being torn away from the renal growth becomes implanted in the wall of the bladder (Sutton).

Villous papilloma in the pelvis of the kidney causes dilatation and pressure atrophy of the organ. The atrophy occurs in little pockets, into which the villi project and may be caught and retained, making it appear as if the growth was primary in the kidney itself.

In the bladder the growth obstructs the urethra if its villous processes are long enough to extend into that tube and plug it. The tumor is apt to be highly vascular, and bleeds spontaneously as well as when injured by instruments introduced for exploratory purposes.

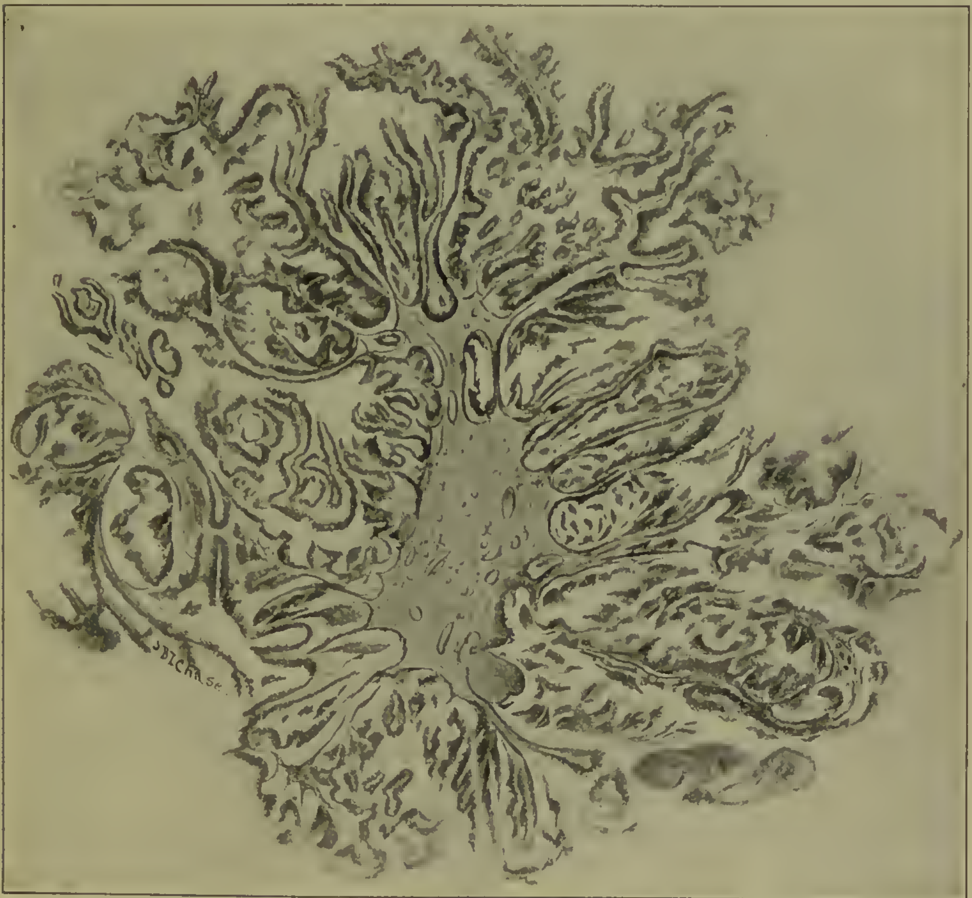

FIG. 105.—Soft papilloma of the large intestine. The magnification is insufficient to show the histologic structure in detail, but shows well the cauliflower-like formation of the tumor. Zeiss, Oc. 3; ob. a′.

(*b*) *Columnar-cell villous papilloma* occurs in the intestine. It forms a cauliflower, dendritic, or villous growth that may attain a considerable size and even obstruct the intestine. It consists of delicate branches that are covered by columnar epithelium. Like the other warts, it is benign, and may at any time soften and spontaneously become detached. Unfortunately, tumors of this form are apt to be associated with some ingrowth of the epithelium, and after spontaneous or surgical removal may continue a malignant growth below the affected surface.

3. **Intracystic villous papilloma** is a rare formation appearing on the walls of cysts, the mammary gland, and ovary. The growths may be very numerous and of small size, or they may be large and cause the cyst to be filled with a delicate villous mass, and later greatly distend it. In some cases the cysts have even ruptured upon the surface of the breast, and the papillary formations continued their growths on the external surface as a form of "fungous hematodes." It is not infrequent to find papillary excrescences on the inner surfaces of the cysts of the paroöphoron, where occasional rupture of the wall of the cyst and continuance of growth are also observed. It is possible that the crowding of the cells which the growth of the papilloma causes disturbs their relationship to the basement membrane, as it is not unusual for growths of this form to become malignant in the course of time.

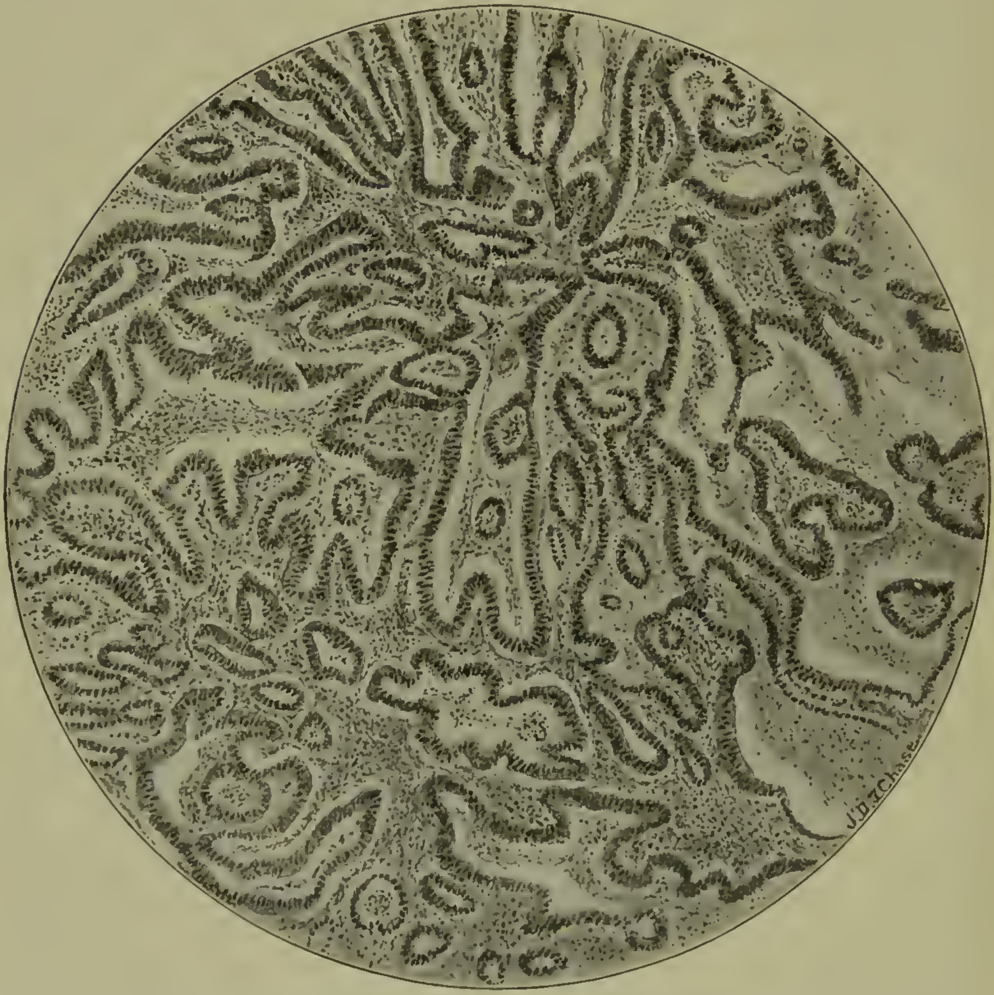

FIG. 106.—Papilloma of the rectum. The section passes through many of the villous projections and presents a glandular appearance. Zeiss, Ob. c; oc. 2.

Pathologic Histology.—In all the papillomata the essential microscopic feature is the persistence, throughout the tumor, of the normal relation of the cells to the membrana propria.

The epithelial cells undergo active multiplication and form exaggerated masses in the hard warts and in the interpapillary processes. Where the cellular prolongations dip deeply into the tumor, interesting formations, known as *epithelial pearls* or "*pearly bodies*," occur from the combined effects of crowding and keratosis.

When distinctly horny, the pearly bodies can be recognized by their yellow color and the absence of stainable nuclei. They can be recognized at all times by their concentric arrangement, the crowded cells being flattened and covering one another very much like the skins of an onion.

Such formations occur only in tumors of squamous epithelium, the columnar cells of the soft papillomata undergoing no keratosis, being, by their shape and the absence of crowding in their soft matrices, prevented from forming the concentric masses.

CUTANEOUS HORNS.

As cutaneous horns, such as occur in man and the lower animals, frequently arise from warts, it seems most convenient to describe them at this point. They have been observed upon the scalp, temple, forehead, eyelid, nose, lip, cheek, shoulder, arm, elbow, thigh, leg, knee, toe, axilla, thorax, buttock, loin, penis, and scrotum.

They may grow from warts, sebaceous cysts, cicatrices, and nails, but it may be impossible to determine, by an examination of the horns themselves, whether they grow from one or the other. The horns formed upon the face and scalp in many cases, probably in the greater number of cases, develop from the sebaceous cysts. They at first consist of the sebaceous matter which projects through a rupture in the wall, and become inspissated upon exposure to the air. From the epithelium about the base the cells grow out upon this firm material until it becomes surrounded by hyperplastic and horny epithelium, which, continuing its growth and undergoing an unusual degree of keratosis, ultimately forms a true horn. Such horns may attain a length of 20 cm. and form startling disfigurements. The *wart horns* are more apt to occur upon the penis and ear, and result from keratosis of the epithelial cells of the tumor. Sutton says that the best way to differentiate between the wart horns and sebaceous horns is to split them longitudinally and see whether or not a cyst is present at the base. *Sebaceous horns* are not rare in mice.

The occurrence of epithelioma in consequence of irregular hyperplasia of the epithelium about the bases of horns is not uncommon.

Cicatricial horns are very rare and usually form on cicatrices resulting from burns. They may grow slowly for many years, and finally spontaneously exfoliate. They may, however, become progressively larger and prove troublesome through accidental partial dislocations which cause painful ulcers and may lead to sloughing. Some remarkable cases have been mentioned by Cruveilhier and Edmunds, in which the horns growing upon cicatrices became so large and proved so offensive as to necessitate amputation.

Nail horns are in reality enormous hyperplasiæ of the nails. They may affect all the nails of the fingers or toes, though they commonly involve only the nails of the great toes. Those which have come under my notice have all been in elderly persons. The great-toe nails may be as large as rams' horns, and are dark in color and irregular on the surface.

EPITHELIOMA.

The epithelioma is a tumor of surface epithelium, resulting from a loss of the normal relationship between the cells and the subepithelial tissue, by which the former descend into and invade the latter.

Two forms are recognized, differing only in the type of cells—*squamous* *epithelioma* and *cylindric epithelioma.* Both tumors are invasive, destructive, and upon occasion metastatic. They are malignant tumors of middle and advanced life.

SQUAMOUS EPITHELIOMA.

This form of epithelioma occurs upon the skin and upon mucous membranes covered with stratified squamous epithelium. It develops only from squamous epithelium, though sometimes one of its essential features (keratosis) is observed in epithelium of other varieties and may lead a careless observer into error.

Seat of Occurrence.—The tumor occurs upon the vaginal portion of the cervix uteri; upon the skin of the face, especially about the lips, nose, and eyelids; in the tongue, penis, labia, vagina, esophagus, cardiac end of the stomach, larynx, bladder, and anus.

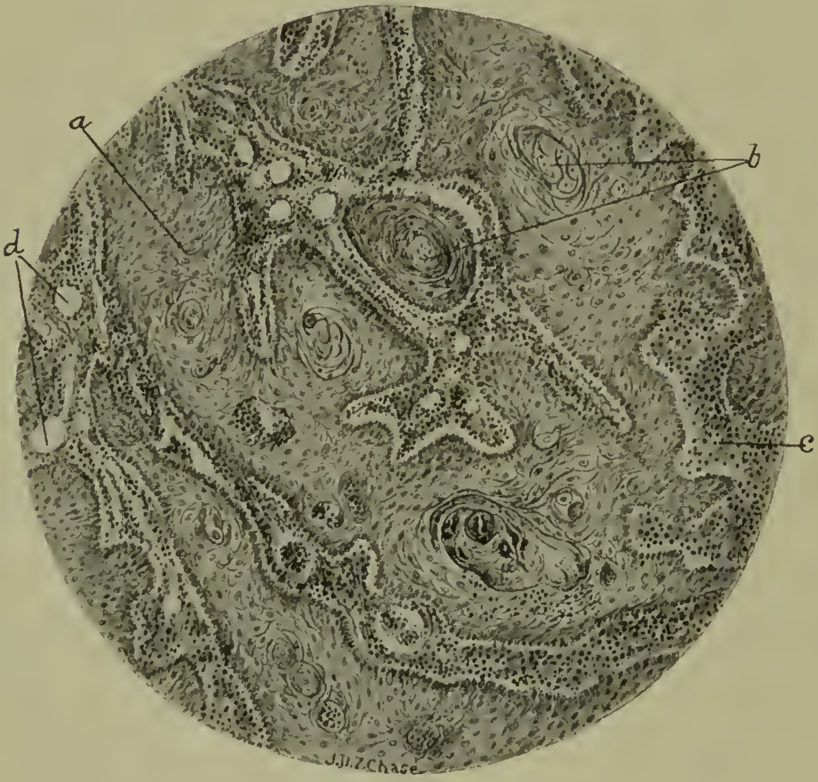

FIG. 107.—Squamous epithelioma: *a*, Epithelial masses; *b*, epithelial pearls; *c*, connective tissue; *d*, capillary blood vessels.

The occurrence of the tumor, especially upon the face, is often preceded for some time by a scaliness and malnutrition of the skin, sometimes by a warty outgrowth. Not infrequently the tumor forms about the bases of horns, warts, lupus-scars, sebaceous cysts, and other unimportant lesions, and occasionally forms in cracks and fissures, though, of course, it is not impossible that the fissures may depend upon the early changes caused by the epithelioma itself. Not infrequently the tumors can be referred to definite mechanical or other irritations, and it will be noted that they usually occur in parts of the body which, because of their position, are particularly prone to injury. Thus, the lips are injured in many ways, and the disease is frequent in smokers, especially when they use clay pipes. The cervix uteri is particularly prone to lacerations in consequence of the stretching to which it is subjected during parturition, and the frequent insults of coition.

Irritation of the skin by soot, paraffin, and tar is found to be a frequent cause of epithelioma, especially of the scrotum, one form of which is known as "chimney-sweeps' cancer."

Epithelioma usually occurs at parts of the body where epithelial tissues of different types meet and where irregularities of development can easily occur—thus, the junction of skin and mucous membrane at the lips, anterior nares, and conjunctival margins; the junction of the skin and mucous membrane of the rectum; and the junction of the squamous and columnar epithelia of the uterus at the cervix. This localization of the epithelioma supports Cohnheim's theory of origin from cellular inclusions or "tissue nests."

Morbid Anatomy.—Sutton finds it convenient to divide the tumors into three chief types: 1. An ulceration with thickened, indurated edges. 2. An ulcer with undermined edges (rodent ulcer). 3. A papillary, warty growth, beneath which the invasion of the tissues occurs.

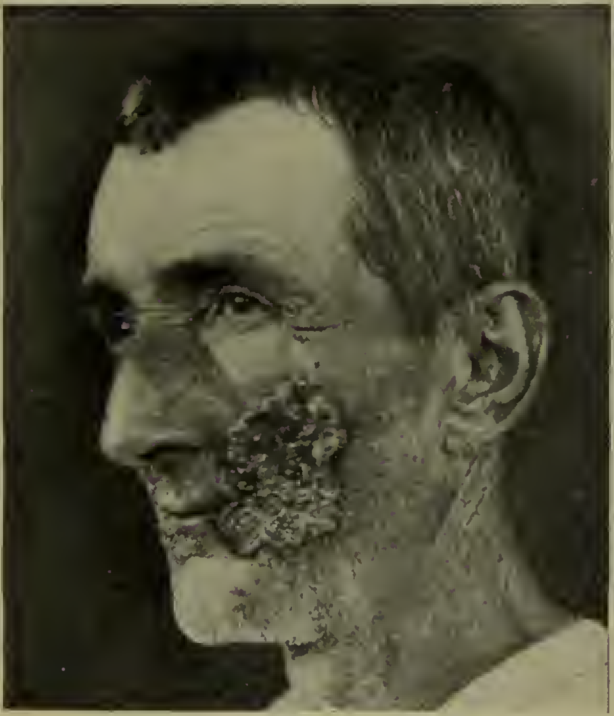

FIG. 108.—Epithelioma of skin (Matas).

All three types are found to be identical in structure when examined with the microscope. If uncomplicated by secondary changes, it is probable that every epithelioma would, when first observed, form a somewhat warty, irregular, indurated papule, and in the papillary form of the tumor this typical form persists. Not infrequently, however, the growth attains only a small size before retrogressive changes appear. Careful scrutiny of almost every epithelioma shows numerous small grayish points upon the surface, which are the beginnings of necrotic descending cellular columns. If pressure be made upon the growth, these softened necrotic cells can be expressed as worm-like cylinders. It is this loss of tissue by necrosis, together with the effect of accidental infection, that determines that the tumor shall ulcerate, and accidental conditions incident upon the tissue destruction whether the resulting excavation shall be superficial or deep. The surface of an ulcerated epithelioma may be covered with a brownish scab if the amount of discharged matter is small and can dry to form a crust, or with a fetid slough if the discharge is more profuse. When once the growth has ulcerated, it becomes infected, and there is little doubt that inflammatory reactions, such as hyperemia, edema, etc., by softening and loosening the texture of the surrounding tissues, predispose to rapid growth of the tumor.

Epitheliomata are never encapsulated ; indeed, it is rare for any epithelial tumor to be encapsulated. It is difficult for one to realize that a lesion whose tendency is to eat away tissue, as the epithelioma does, is really a tumor, though the microscopic examination shows that, in spite of the loss of tissue, a progressive though abnormal increase of epithelial tissue is constantly going on.

A section through an epithelioma shows its substance to be quite mixed. The normal subcutaneous tissue appears yellowish from the presence of fat. In it are what appear to be an increased number of fibrous trabeculæ, and in and between these the epithelial cell columns and nests occur as pinkish clusters. The invaded tissue is dense and hard.

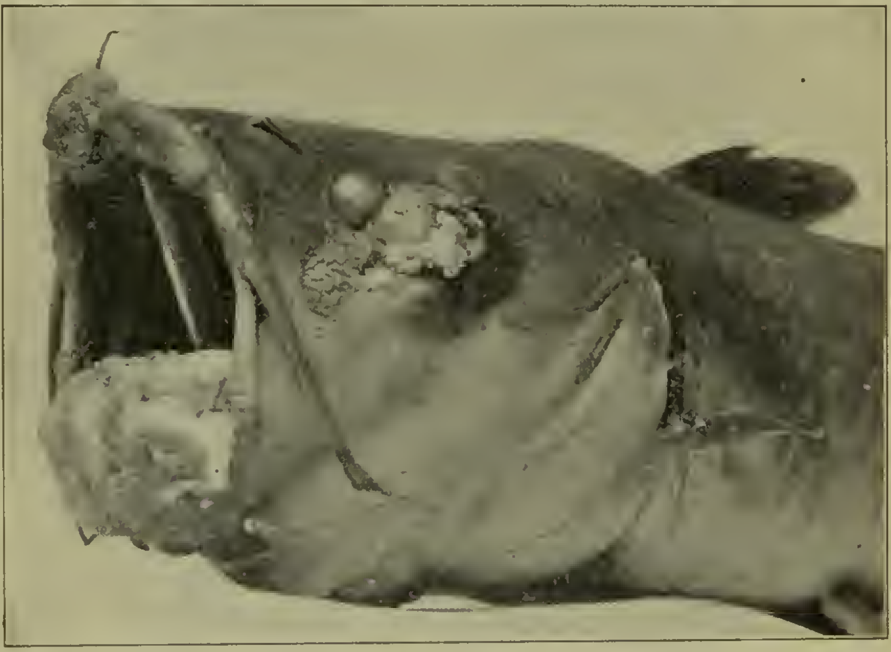

FIG. 109.—Papillary epithelioma of a white catfish.

Pathologic Histology.—All epitheliomata are histologically similar. The growth consists of an extensive hyperplasia of the epithelium, which descends in trunks and branches from the skin above to ramify in all directions through the subcutaneous or subepithelial tissues. Serial sections of the tumors show these epithelial masses to be associated and united by intermediate cellular bands, so that the structure really resembles an inverted cauliflower or coral growing into the deeper tissues.

The cells are for the most part larger than normal, contain comparatively small, faintly staining nuclei, frequently show numerous "prickles" upon their surfaces, and commonly contain droplets of keratin. In skin tumors there are numerous "nests" or crowded groups of cells in which the keratosis characteristic of the horny epithelium of the skin takes place and forms the same "epithelial pearls" or "pearly bodies" that were described as occurring in the similar crowded cells of the papilloma.

The epithelial pearls are yellowish in color and consist of concentrically

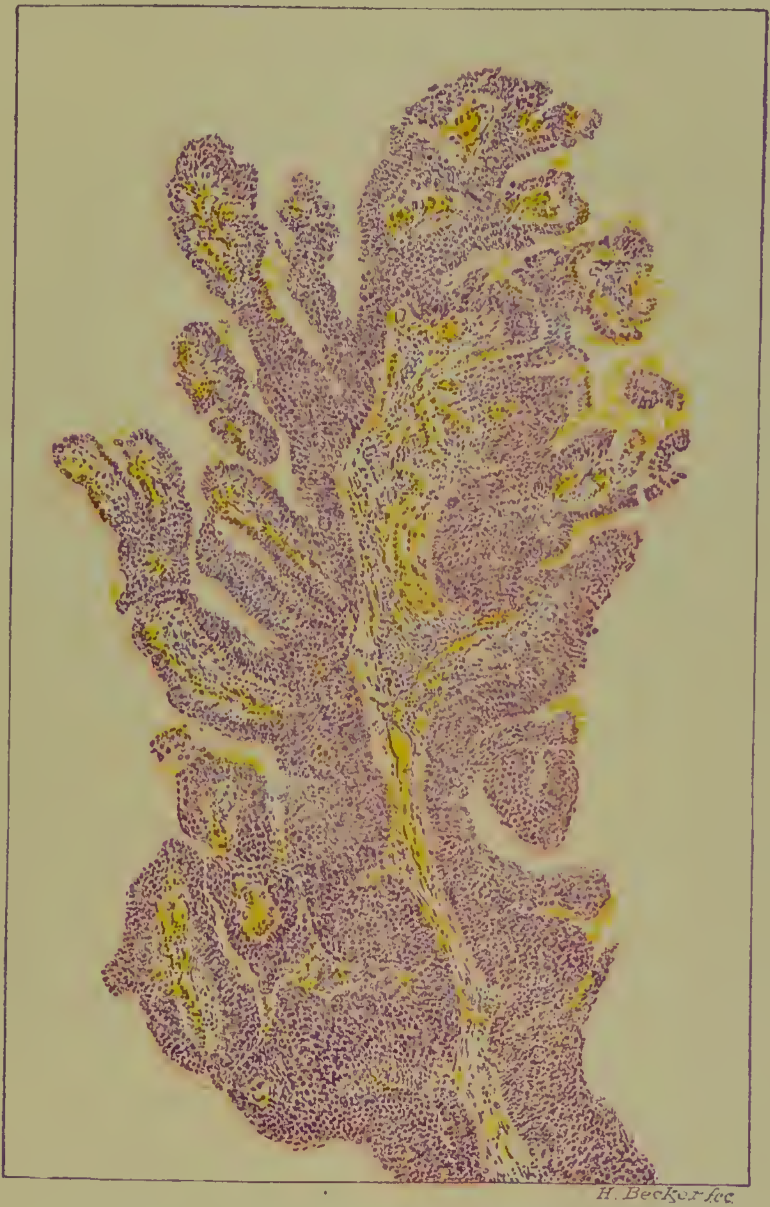

FIG. 110.—Squamous-cell carcinoma of the cervix; finger-like processes arising from a common stem. × 80 (Cullen). Traversing the center of the specimen is a delicate stem of connective tissue, in the center of which is a blood vessel. This stem gives off lateral branches, which likewise contain blood vessels. The main stem is covered in some places by only one layer, in others by many layers, of squamous epithelium. The epithelial cells next to the stroma tend to be cuboidal. The epithelial nuclei throughout are fairly uniform in size. Near the left lower corner are several cross-sections of the terminal branches or fingers. These present a typical appearance.

arranged masses of cells. Between the cells is an ordinary areolar tissue, upon which the descending masses of cells abut, or upon which they may stand in orderly fashion. This areolar tissue carries the blood vessels and lymphatics which formerly nourished the skin, but now nourish the tumor. There are some indications of infection of this tissue, as a rule, and it may be infiltrated with leukocytes. Local areas of infection may occur at points remote from the tumor itself, by bacteria conveyed through the lymphatics. It is partly from the presence of the bacteria, though chiefly because of malnutrition, that the necrotic conditions arise.

Growth and Tendencies.—The squamous epithelioma shows the greatest variation in the rapidity with which it grows and the time at which metastasis occurs. Latent forms having lasted for years are frequently seen upon the faces of old people. I was once consulted by a man, aged eighty-eight years, in regard to a latent epithelioma beneath the left eye that had attained the size of a silver dollar. It was covered with a brown crust, its borders were not infiltrated, there was no trace of inflammation, and I learned that the tumor had existed for thirty years without further discomfort than arose from its unsightliness.

Such slow-growing epitheliomata occur chiefly about the nose, ear, and eyelids, and are sometimes spoken of as *epithelioma exedens*, *cancroid*, and *Jacob's ulcers.*

Another form of rodent ulcer begins as a small papule whose growth, though slow, is steadily progressive and destructive, resulting in extensive loss of tissue and hideous deformity.

As experience has shown that interference with such tumors arouses them to more active growth, they were called by the older surgeons "*noli me tangere.*" In marked contrast to these are the common epitheliomata seen daily in large clinics. Such tumors, occurring upon the lip, penis, or cervix uteri, grow progressively and call for surgical interference in the course of six months or so. After removal they frequently return, and after a year or two metastasis to the lymphatic nodes is observed. The glands enlarge, soften, and ultimately open, leaving necrotic material to escape externally from a gaping wound, or internally into the peritoneal or some other cavity. Death results, after a year or two, from hemorrhage from the erosion of blood vessels, pressure upon vital parts, or infection. Still more marked is the contrast with minute and often entirely unobserved tumors of the pharynx and tongue, which cause metastasis with enormous secondary growths in the lymph nodes, while they themselves still remain unobserved.

The termination of epithelioma, therefore, varies in different situations. In the larynx it may lead to death from pneumonia, caused by the inhalation of the infectious matter. In the esophagus it may lead to perforation of a bronchus and death from pulmonary gangrene. In the uterus it may cause slow death after invading all the pelvic organs, obstructing their outlets, and occasioning great suffering. In the tongue it may rapidly invade the lymphatic glands of the neck and cause death from suffocation.

Thorough eradication of the tumor while still small and before metastasis has occurred may effect a perfect cure.

The metastasis of epithelioma is chiefly lymphatic, and is easily understood when one remembers that the cells descending into the subcutaneous and submucous tissues and scattering through them really occupy the lymphatic spaces of the tissue. When the cells of the tumor gain entrance to the veins, hematogenous metastasis to the lungs may occur.

CYLINDRIC EPITHELIOMA.

This form of epithelioma results from the invasion of the tissues by columnar epithelium from the mucous membranes. As it also appears to develop from the glandular tubules so widely disseminated throughout the membranes, the cylindric epithelioma is simply one form of *adenocarcinoma* (*q. v.*) and needs no separate description. It occurs in the pylorus of the stomach, in the cecum, sigmoid flexure, and rectum. It has sometimes been described as a malignant or destructive adenoma.

The cylindric epithelioma is less marked in its metastasis than the squamous form, and the uterine tumors in particular are very slow to give metastasis.

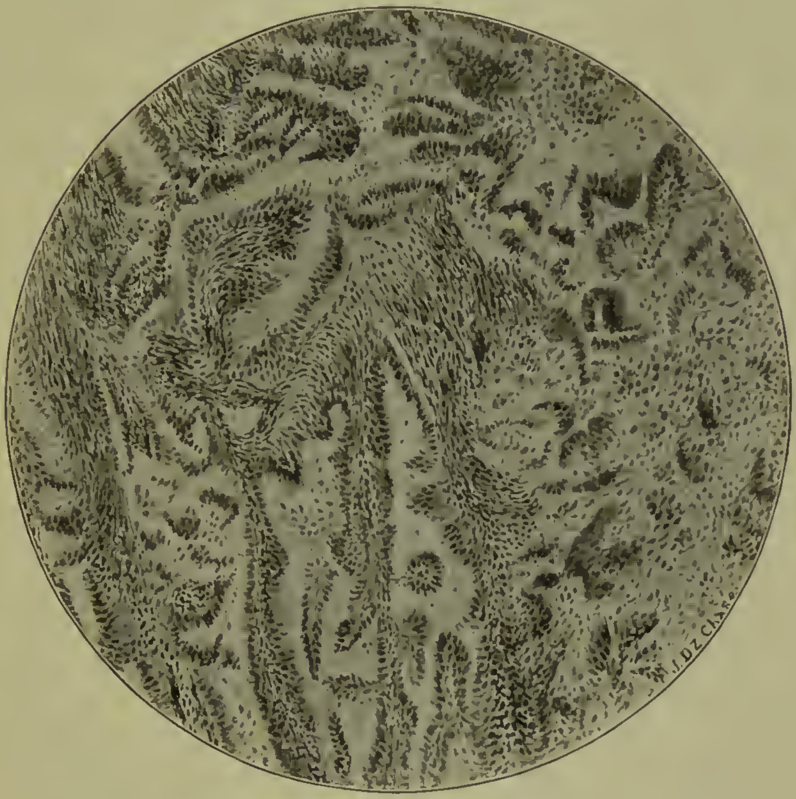

FIG. 111.—Cylindric epithelioma of the uterus. The section was taken from a fragment of the fundus of the uterus. Zeiss, Ob. c; oc. 2.

The secondary tumors are characterized by the presence of columnar cells whose histogenesis can sometimes be determined by careful study.

CANCER OR CARCINOMA.

Cancer or carcinoma is a malignant tumor resulting from a progressive infiltrative hyperplasia of epithelium. Such an infiltrative hyperplasia of epithelium is necessarily accompanied by loss of that relationship of epithelial cells to the membrana propria apparent in all typical epithelial organs and by a heterogeneous invasion of the tissue interstices by the growing cells. A few writers still speak of epithelial and connective-tissue cancers, the former being the true cancer, the latter, the sarcoma.

The true cancer develops solely from epithelium, and can be primary only in tissues and organs containing epithelial cells. It is, therefore, essentially a tumor of epiblastic and hypoblastic derivatives, though the occurrence of such growths in the mesoblastic epithelium of the genito-urinary apparatus somewhat lessens the embryologic limitations that can be placed upon them. The puzzling occurrence of carcinomata in mesoblastic tissues is to be accounted for in part by assuming that they are secondary and metastatic, and in part by supposing that they are *endotheliomata* mistaken for carcinomata, the resemblance of these two tumors being so great at times as to make their differentiation possible only after careful study.

Seat of Occurrence.—According to the form of epithelium from which they originate, the cancers may be divided into *epithelioma*, which grows from the flattened surface epithelium; and *adenocarcinoma*, which develops from the epithelium of glands. The *cylindric epithelioma* develops chiefly from the tubular glands with columnar epithelial cells, and is a form of *adenocarcinoma*. The *epithelioma*, which has already been described, develops from the skin and from the mucous membranes of the mouth, larynx, esophagus, cervix uteri, vagina, bladder, and anus.

The adenocarcinoma may arise as a primary tumor in the mammary gland, in the cervix and corpus uteri, pylorus, skin, sigmoid flexure, colon, esophagus, ovary, testicle, penis, labia, pancreas, larynx, thyroid gland, liver, kidneys, bladder, prostate, sebaceous and sweat glands, bronchial glands, and other epithelial tissues.

As secondary growths, cancers of all kinds usually appear in the lymphatic glands, next most frequently in the liver, then in the lung. They also occur in the spleen, brain, spinal cord, bones, cartilage, and serous membranes.

Pathologic Anatomy.—**Morphology.**—Scarcely any neoplasm is as variable in morphology as is the carcinoma. In some cases it forms a distinct tumor, which grows with varying rapidity and attains considerable size; thus mammary carcinoma may attain the size of a man's head. In other cases the growth of the epithelial cells is accompanied by such a series of local disturbances in the way of fibrosis, degeneration, necrosis, ulceration, and cicatrization that though it may persist for years, no enlargement results, and the general appearance is that of a chronic ulceration or cicatrization rather than that of a tumor.

Some carcinomata form nodes of irregular, rounded, and nodular shape, rarely circumscribed, but usually characterized by irregular fibrous extensions, which proceed in various directions and appear to distort the organ by traction and pressure.

Other tumors have no nodular form, and resemble irregular cicatrices in the organ, drawing it together and greatly disturbing its size and form as well as causing atrophy of its substance.

Still other tumors, among which are mammary, gastric, and dermal cancers, especially when superficially situated, are characterized by loss of tissue through ulceration, and present the appearance of excavated ulcers with indurated edges and elevated borders. From the ulcerations exuberant granulations may grow, later becoming infiltrated with the carcinoma cells, developing into large *fungous hematodes*, which project as red, granular, bleeding, or suppurating tissue masses.

It is thus evident that there is very little uniformity in the appearance of carcinoma, and its multiplicity of forms would sometimes make its recognition difficult were not certain tissues more predisposed to it than to other forms of neoplasm.

The texture of a carcinoma varies with its structure; some consist of soft, encephaloid, cellular tissues; others largely of dense cicatricial connective tissue.

Structure.—When a carcinoma is divided and the cut surfaces are examined, a variegated appearance is presented in most cases, the pinkish cellular tissue of the carcinoma, whitish stroma, and intermediate fatty tissue, or tissue of the organ affected, contrasting distinctly. When the tumor is pressed and scraped, it yields "cancer juice" or "*suc cancereuse*," a milky fluid which, under the microscope, is found to consist of a serous fluid containing large numbers of epithelial cells.

Cysts not infrequently occur in carcinoma, being formed either by local softening of the tumor tissue or by obstruction of the glandular ducts, etc.

The cut surface usually shows the tumor to be entirely uncircumscribed, devoid of the least semblance of a capsule, and made up of nodular masses with invading prolongations ramifying in all directions. If the growth be superficial, it is commonly umbilicated or depressed in the center, this being especially well shown in the secondary carcinoma nodules of the liver. Mammary carcinomata usually show a marked depression and retraction of the nipple.

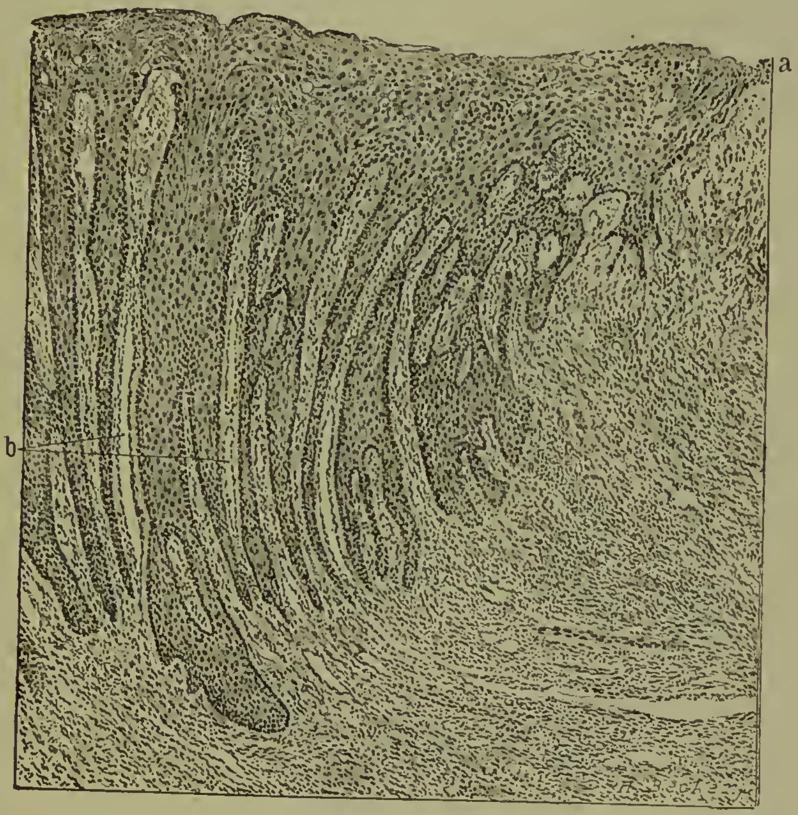

FIG. 112.—Changes in the epithelium along the margin of a squamous-cell carcinoma of the cervix. × 56 (Cullen). Just to the right of this section (at *a*) the epithelium has invaded the cervical tissue in all directions, giving the typical picture of squamous-cell carcinoma. In this drawing it is noted that the surface of the mucosa is comparatively even, there being no outgrowths. The stroma has been invaded to a considerable depth by the epithelium. The epithelial cells, however, are uniform in size, present the usual appearance, and even in the deep or cuboidal layer are still sharply defined. The lengthening of the papillæ is due to the downgrowth of the epithelium, as they do not project from the surface. The clear spaces indicated by *b* represent delicate blood capillaries. The underlying stroma is normal, showing no signs of infiltration. Although the picture might at first sight be suggestive, there is no evidence of a malignant growth in this section.

Pathologic Histology.—The structure of all carcinomata is essentially the same, though the conditions of development and secondary degenerations modify their general appearances. The tumor consists of *stroma* and *cells*.

The **stroma** or **matrix** of the tumor is composed of a well-vascularized fibrous tissue, containing a considerable number of elastic fibers. The stroma, no doubt, consists in large part of pre-existent connective tissue, though in scirrhous tumors much additional tissue must be formed. It can safely be said that the development of the stroma is as much a part of the growth of the carcinoma as is the proliferation of its cells, for no matter where we find the growth, we find the stroma in about the same relative proportion for the particular tumor under study. When carcinoma takes on a secondary metastatic growth in the lymphatic nodes, which contain so little connective tissue, the growth of the cells of the lymphatic embolus is immediately accompanied by the formation of a new fibro-elastic stroma.

The proportion of stroma to cells varies remarkably in different cases, no adequate explanation for the difference having yet been discovered. Those tumors in which there is little stroma in proportion to the number of cells are known as *encephaloid* or "soft cancer"; those in which there are much connective tissue and few cells are called *scirrhus*, or "hard cancer."

The stroma can be freed of its contained cells by spreading out a freshly cut section and brushing it with a camel's-hair pencil, or by placing it in a test-tube with water and shaking.

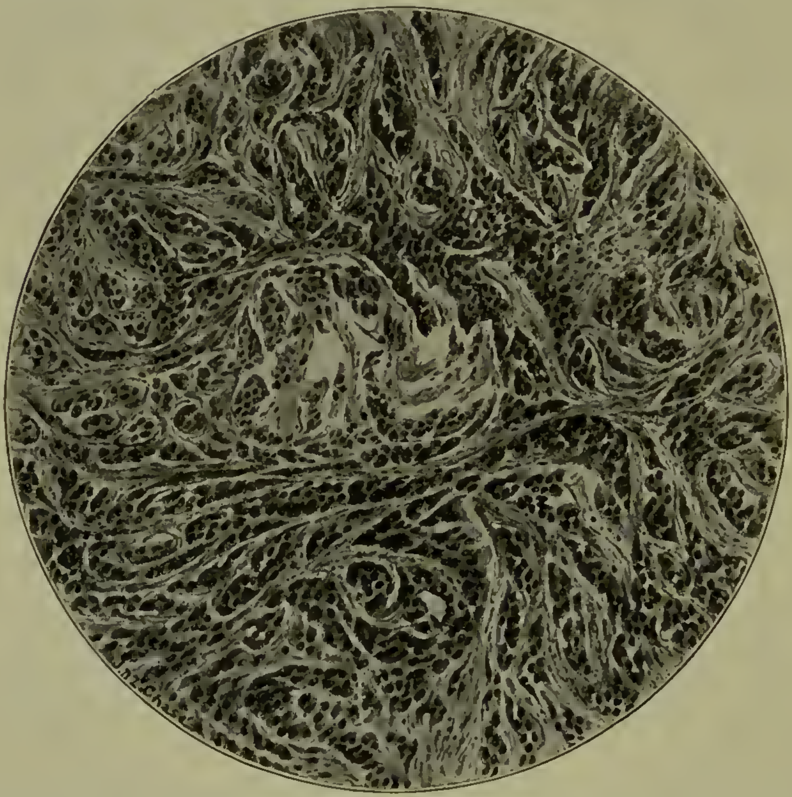

FIG. 113.—Scirrhus carcinoma of the mammary gland. The section passes through a relatively cellular part of the tumor and shows the bizarre arrangement of the cell-nests among the radiating and reticulated connective-tissue framework. Oc. 4; ob. 3.

The carcinoma stroma is always rich in lymphatics, or in spaces communicating with the lymphatics, and, indeed, it might safely be said that all the alveolar spaces of the tumor belong to its lymphatic system.

Nerves are also present, though in small numbers, and can be found with difficulty. Their presence, no doubt, accounts for the great pain with which the development of the tumor is sometimes attended.

The **cancer cells** are the progeny of the epithelial cells of the organ affected, which are stimulated to unusual proliferative activity by the as yet unknown cause of the tumor, multiply rapidly and escape from their normal environment into the lymphatic spaces and channels—*i. e.*, the tissue interstices—where they grow without restriction. The nearer they are to their parent cells, the more closely they resemble them; the more remote they become, the more nearly they revert to the primitive, spherical, undifferentiated embryonal cells. There is considerable variation in this particular in different tumors. Thus, the cylindric or columnar cells may retain their shape regardless of the growth and extension of the tumor, and change so little that even in the secondary metastatic tumors their histogenesis may be apparent. Primitive tendencies of the cells may be retained by their progeny and manifest themselves wherever they appear, so that cells of uterine and gastric carcinomata with a tendency to undergo colloid metamorphosis may form colloid masses in the lung, liver, or any other viscus to which they happen to be transported. These characteristics are so constant that in most cases a microscopic examination of a secondary nodule in the liver may at once inform us whether the cells were derived from the pancreas or stomach, and the examination of a nodule in the lung may show keratin formations with epithelial pearls if the cells come from the skin, cylindric cells and alveolous formations if from the alimentary apparatus, or masses of spherical cells if primary in the mamma.

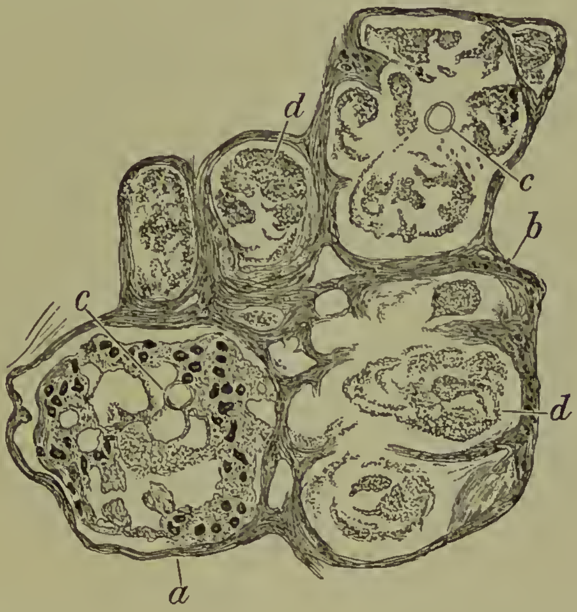

FIG. 114.—Colloid carcinoma (Weichselbaum): *a*, Epithelial cell-nests in which cells are still visible; *b*, connective-tissue trabeculæ undergoing mucous metamorphosis; *c*, *c*, drops of colloid formed by metamorphosis of epithelial cells; *d*, granular débris of destroyed cells.

The cells of carcinoma vary in size according to their histogenesis. For the most part they show the usual characteristics of epithelium, having a considerable relative quantity of cytoplasm and distinctly vesicular, usually ovoid, nuclei, which stain palely. Being aggregated in "nests" or clusters, the cells rarely have an opportunity to show a perfect form, but are flattened by mutual pressure and become polyhedral. When the cells are actively proliferating, mitotic figures are numerous. The mitoses, while no doubt usually progressing normally, frequently show irregularities, with the occurrence of large, deformed, and often giant nuclei. Giant cells of immense size, with one or more large nuclei, are sometimes observed and are called *physalides*.

The cells seem to yield to pressure, and one cell frequently sinks deeply into its neighbor. It even appears as if one cell might be taken entirely into the substance of another, a condition which the older writers looked upon as an exhibition of endogenous cell formation, but which has recently been regarded as an evidence of phagocytic activity of the cells. Leukocytes are also commonly contained within the cancer cells and are believed to have been swallowed by them. Other interesting and peculiar cellular inclosures are observed, many of which may be undescribed forms of cellular degeneration or cellular activity; others possibly are parasites.

There is no recognizable intercellular substance, and the cells do not cohere, but can readily be penciled from the stroma in which the nests are contained. The looseness of the carcinoma cells in their matrix is one of the chief differential features between epithelial and endothelial growths. In endothelioma the tendency is for the cell clusters to hang well together and to cling to the surrounding connective tissue.

The degenerations of the cancer cells are identical with those of their antecedents. As has been already shown, the squamous cells show their usual tendency to cornify, the change being best seen in the epithelial pearls. Calcareous infiltration sometimes occurs in the epithelial pearls. The columnar cells originating from the mucous membranes and glands undergo colloid (colloid cancer) and mucoid (carcinoma gelatinosa) metamorphosis. The cells of mammary cancers sometimes undergo fatty metamorphosis, presumably from the pressure of the stroma, though it may be the sign that the cells of the gland normally provide fat globules for the milk by degeneration. In the cancerous hypernephromata the adrenal cells show both fatty and glycogenic infiltrations. Calcification and myxomatous degeneration are frequent in the stroma of carcinoma. Melanocarcinoma is a form characterized by pigmentation of the cells. It usually develops upon the skin. It closely resembles melanotic sarcoma, but can be differentiated from it in most cases by its early metastasis to the lymphatic glands.

The cells of carcinoma may be damaged by toxic processes common to the whole body, and cloudy swelling and other toxic changes may be observed under appropriate conditions.

Serous infiltration of the carcinoma cells is not uncommon and causes an enormous increase in size and vacuolation. It may be because of such retrogressive changes that the " physalides " occur.

Inflammation in carcinoma occurs precisely as in normal tissue, and the occurrence of secondary inflammations in consequence of superficial ulceration with infection is frequent. Necrosis of carcinoma tissue is frequent in consequence of malnutrition, infection, etc.

The **architecture** of carcinoma is extremely simple, all tumors of this genus following the same general type, the cells occurring in irregular nests or alveoli in the stroma, in the loose manner described. Serial sections of carcinoma nodules reconstructed on a large scale by the paraffin method show that all the cell nests connect with one another by intermediate cellular extensions or bridges, so that the entire nodule, and probably the entire tumor, consists of a single ramifying, branched, coral-like, or cauliflower-like mass of epithelium, inclosed on all sides by the stroma.

One can conceive of the growth, therefore, as resembling the roots of a plant and extending in all directions, growing cell by cell in the direction of least resistance, each cell added paving the way for the addition of others by increasing the size of the interstices of the stroma.

The growth of the tumors seems to take place from the alveolar structure of the affected glands, probably from several different foci, though this can no longer be determined after the tumor has developed. Study of the apparently healthy parts of carcinomatous mammary glands has shown that every carcinomatous gland is a diseased gland throughout, all parts manifesting catarrhal or other morbid conditions.

In the atrophic mammary glands of old women the development of the carcinoma from the alveolar tissue becomes almost impossible because of the disappearance of the acini and their cells, so that such cancers develop chiefly from the ducts in which the epithelial cells proliferate, forming great masses which fill and distend them before they finally escape into the interstices of the gland. Cancers having this origin are usually sufficiently characteristic to be readily recognized, and have been called, especially by English writers, "*duct carcinoma.*"

Disposition and Clinical Features.—Cancers are almost invariably highly malignant tumors. The persistent invasion of the organ by the columns of growing cells and the development of the fibroconnective-tissue stroma are accompanied by progressive atrophy of the proper substance of the organ, so that, little by little, it becomes transformed into the neoplasm. The extension of the loosely attached and actively vegetative cells into the primitive, and perhaps in many cases into the large lymphatic, channels predisposes to an early transportation of the tumor cells to the related lymphatic nodes, where secondary tumors are formed. It is surprising how early this *metastatic distribution* occurs, in some cases taking place as soon as a noticeable growth is formed or prior to its detection. It sometimes happens that a primary growth, so insignificant that its presence has not yet been detected, may so invade the related lymphatic nodes that the secondary tumors become of paramount importance. This early invasion of the lymphatics and tendency to metastasis are very important matters from a prognostic point of view, upon which the surgeon cannot lay too much

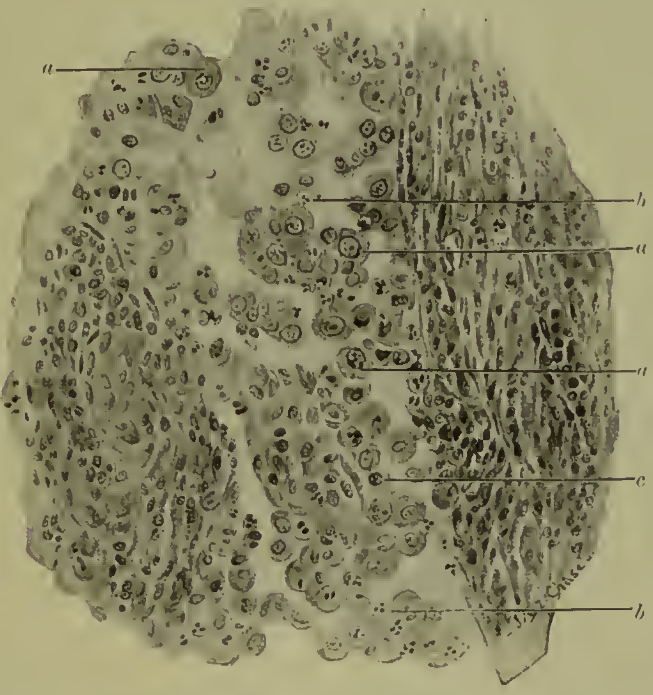

FIG. 115.—Carcinoma of lymphatic node, illustrating the cause of metastasis. On the right and left are portions of glandular substance with interstitial fibrous change. Through the center, from top to bottom of the illustration, there is a widely dilated lymph vessel filled with cells: *a, a, a,* Carcinoma cells freely circulating in the lymph; *b, b,* leukocytes; *c,* lymphocytes. Oc. 2; ob. 9.

stress, for to remove a cancer from a mammary gland always means rapid recurrence of the growth from uneradicated cellular prolongations, and removal of the entire breast may be succeeded by an equally prompt return of the tumor in neighboring already infected lymphatic nodes. It is upon this active metastatic tendency and our inability to gauge it that complete extirpation of the diseased organ, the subjacent muscles, the suprajacent skin and subcutaneous tissue, as well as the entire system of lymphatics,—axillary and supra- and infraclavicular,—has been so successfully practised.

The metastasis of carcinoma takes place through the lymphatics first, but sometimes later through the blood. Blood metastasis is seen particularly in abdominal tumors, and especially in those of the digestive organs, which early seem to distribute through the portal circulation, so that metastatic cancer of the liver takes place early. In mammary cancer as well as in other superficial forms of the disease the conditions seem more favorable to lymphatic extension, and the lymph nodes are invaded one after another, a long time elapsing before hematogenic metastases appear. It seems as if the cancer emboli reached the streaming blood in these cases by way of the lymphatics, though it is always possible that the veins are in some way involved and direct communications set up. The communications between the veins and lymphatics of the abdomen also predispose to the entrance of cancer emboli into the circulation. . The secondary nodes thus originated usually occur in the lungs, showing that they reach the venous blood first, and that it is in the pulmonary capillaries in which the cellular emboli are retained. Occasionally a broad generalization of the tumor occurs, possibly by the passage of the cells through the pulmonary filter and their entrance into the general systemic circulation. The occurrence of secondary nodes is then possible in all parts of the body, and they may be found in the lungs, liver, spleen, kidneys, brain, spinal cord, bones, serous membranes, muscles, and other tissues.

Recurrent carcinoma, or carcinoma reappearing after excision, is identical with the primary tumor, except that the cicatricial tissue resulting from the operation modifies the conditions of growth by substituting extremely dense for the normal loose tissues. The recurring tumor, therefore, usually avoids the cicatricial tissue or makes but little inroads into it unless the return is immediate and makes good headway before the cicatrix has contracted.

Upon the surface of ulcerations, such as occur over cancers, as well as in operation wounds made for their removal, the granulation tissue frequently becomes invaded by the proliferating cancer cells, which find favorable conditions for growth in the loose, well-nourished granulation tissue. This associated growth of the carcinoma and granulation tissue leads to the formation of fungous masses (*fungus hematodes*), which are red, bleeding, sloughing formations, covered with a foul secretion and subject to superficial necrosis with frequent severe hemorrhages. Sometimes after operation the skin becomes rapidly invaded by the cancer and extensive areas become thickened, nodular, darkened, and edematous. Such superficial invasions from a mammary cancer may extend over a large part of the chest and arm, and have been described by French authors as "*cancer en cuirass.*"

The superficial ulceration sometimes gives place to deep excavations in the tissues, from which hemorrhages may take place from rupture of thinned vessels, though thrombosis usually closes the vessels as the cancerous process invades them. Examination of the portal system in abdominal cancers will frequently reveal a thrombus in one of the venous trunks, sometimes with its invading cancer cells, which have entered a disorganized vein near the focus of active disease.

In addition to their local manifestations many cases of cancer are associated with *cachexia* or nutritional depravity, the nature of which is not yet understood. How a local disease, or in metastatic cancer a series of local disorders, can produce cachexia has not yet been determined, but in all cases in which cancer persists for a long time the patient falls into profound anemia, with a yellowish or greenish-yellow tinge of the skin, general wasting and asthenia, and sometimes slow death from general weakness. It has been thought that this is the result of the apprehension and pain suffered by the patient, and in some cases it has been referred to loss of blood, but it occurs in cases of concealed cancer without the presence of either of these conditions to explain it.

It is held by some that cachexia results from metabolic disturbances resulting either from the loss of some internal secretion no longer furnished by the disorganized gland or from the pressure of an excessive quantity of some ferment or other product of the numerous and active epithelial cells.

Pathology of Cancer.—The exciting cause of carcinoma being unknown, it is difficult to explain all its peculiarities. Its occurrence is frequently preceded by mild and comparatively unimportant lesions. Thus, the skin cancers seen in chimney-sweepers and in tar and paraffin workers are commonly preceded by a peculiar form of chronic eczema, caused by the irritation of the substances with which they come in contact in their work. The cancer of the tongue of smokers is also preceded by whitish patches (*leukoplakia lingualis* or *buccalis*) occurring about fissures and ulcerations of the mouth.

Skin cancers also occur from changes about the bases of warts, horns, irritated sebaceous cysts, and other pathologic conditions of the skin. Cancers of the deeper organs sometimes arise from the borders of ulcers. This seems to be especially true of the stomach, where pyloric ulcers are supposed to be sufficiently irritated by the passing food to be stimulated to carcinoma growth. It is, of course, not impossible that ulcerations of this form, though appearing to be simple ulcers, are really carcinomatous ulcers from the very beginning. In the cervix of the uterus the growth of carcinoma is apt to begin about lacerations resulting from previous childbirth, where an abnormal development of epithelium occurs in the attempt to cover the gaping fissure.

Carcinoma development seems to be a peculiarity of the individual in most cases; a peculiarity of the species in all cases. There are many cases in which one patient will have many cancers—all primary and independent growths—in different parts of the body. Both breasts, the stomach, and the uterus, for example, may be simultaneously and independently affected.

A cancer in one part of the body is not only capable of dissemination by the natural metastatic channels, but can be implanted in other parts of the body of the same individual. Thus, ulcerated cancers of the mammary gland sometimes cause ulceration of the arm of the same side which comes in contact with it, and into these ulcerations, through repeated contact, the cancer cells become implanted and grow. From carcinomata small pieces have been excised and implanted into remote parts of the subcutaneous tissue of the same individual, with the result that they have grown and produced implantation tumors. All experiments in which carcinoma fragments from one person have been implanted into other normal individuals have, however, failed. Further, every attempt thus far made to implant a human carcinoma into one of the lower animals has failed.

Cancers (squamous epitheliomata) occurring in white rats have, however, been successfully implanted into other white rats by Hanau, and a peculiar sarcoma of white rats has been successfully implanted generation after generation into other rats by Loeb.

These peculiarities of the tumor indicate that it is an abnormality of the individual, or in the case of rats of the species, that permits the carcinoma cells to invade the tissues.

As carcinoma is shown to be non-inoculable, it seems to follow that it is non-contagious, and a study of the literature will satisfy one that the evidences of contagion are extremely slight. Though cancer of the cervix uteri is very common among married women, cancer of the glans penis among their husbands is very rare, only about a dozen cases of apparent transmission of this kind being on record.

Etiology of Carcinoma.—The etiology of carcinoma is very obscure.

I. **Predisposing Causes.**—1. *Heredity.*—There is little doubt but that heredity plays an important part in the etiology of carcinoma. It is largely a family disease, and while spontaneous cases may occur at any time, a careful questioning will in most cases elicit the fact that near relatives of the patient have suffered from the disease.

2. *Age* has a pronounced influence in its occurrence. It is essentially a disease of middle life, and though cases sometimes occur in early adult life, and rare cases are seen during adolescence, they form marked exceptions to the rule that carcinoma is rare before the thirty-fifth year.

3. *Race.*—Caucasians are more predisposed to carcinoma than the other races of mankind. It affects all human beings, however, and is not at all uncommon among the lower animals, nearly all of which may suffer from it.

4. *Sex.*—Carcinoma is more frequent in women than in men, because of the larger size and greater activity of certain of the epithelial organs of women. Thus, cancers of the mammary glands and uterus are very common in women. Cancer of the mammary gland is very rare in men, who frequently, however, suffer from carcinoma of the stomach, pancreas, rectum, liver, lip, and larynx.

5. *Geographic distribution* seems to have some influence upon the occurrence of carcinoma. It occurs more frequently in temperate than in tropic or arctic climates, and seems to have some preference for low, damp, wooded, alluvial districts with a clayey soil.

6. *Occupation* has some influence, by bringing individuals into contact with substances which irritate the skin. Of these must be mentioned soot, tar, and paraffin. For many years it has been known that chimney-sweepers suffer from an epithelioma of the scrotum that is rare among other persons, and recently it has been found that tar and paraffin handlers are also more subject than others to skin cancers. Sutton has found, however, that the wives of chimney-sweepers are also more commonly affected with cancer than women in general, a matter that meets with no ready explanation.

II. **Exciting Causes.**—1. *Irritation.*—That irritation and injury are in themselves sufficient causes of carcinoma seems to be doubtful. The fact that cancer of the lip should be so common in men and so rare in women, supported by the fact that it is usually the men and not the women who smoke, that the occurrence of this form of cancer is often preceded by fissures and cracks just where the clay pipe produces its irritation, appears convincing when taken by itself, but it seems to be offset by the fact that so few cases occur in spite of the immense number of smokers, and that it is not rare among men who do not smoke.

The fact that cancers commonly occur at parts of the body at which frictions and traumatic injuries are frequent—mouth, larynx, esophageal entrance to the stomach, pylorus, rectum, cervix uteri, vulva, and mammary gland—suggests that in all these situations it is the irritation that stimulates the cells to activity.

This must, however, be accepted with reserve, as it is at these very situations that we find the transition of skin to mucous membrane, squamous epithelium to columnar epithelium, and developmental defects that may escape observation, all of which may be associated with conditions favorable to the development of carcinoma.

2. *Altered Resistance of the Connective Tissue.*—Ribbert has advanced an interesting though doubtful theory which accounts for the growth of the tumor upon a change in the connective tissue rather than upon activity of the cells. He thinks the connective tissue, losing its normal resisting power and becoming looser than normal, draws apart the cells forming the membrana propria and permits the epithelial cells to take on the unrestricted growth which produces the tumor.

In all cases marked changes in the connective tissue are evident, the cancer "stroma" being thus formed, and it may be truthfully said that the connective tissue grows into and among the cells quite as often as the cells grow into the spaces of the stroma. It is, however, difficult to conceive of so indifferent a tissue as the cancer stroma playing the chief rôle in the formation of a tumor whose very essence seems to depend upon cellular activity, and whose cells, when transported to the lymphatic glands, proceed to continue the same unrestricted multiplication that we observe in the primary tumor.

3. *Infection.*—There are many peculiarities about carcinoma that make it resemble an infectious disease, and, indeed, it may be one, though it has other equally marked peculiarities which are entirely different from those of any other known infectious process. The infectiousness of carcinoma has received so much attention during the last quarter of a century that an enormous literature upon it has developed and many facts of interest have been collected.

Bacteria and Carcinoma.—The study of the bacteriology of carcinoma was begun quite early, and although the greater number of investigators failed to find bacteria in the healthy parts of the tumor, claims were made as early as 1885 by Brault that the tumors were of micro-organismal origin. This opinion was further supported by Rappin, in 1887, who, like Brault, succeeded in cultivating a diplococcus which was regarded as specific. Schill probably cultivated the same coccus. More attention was attracted to the discovery of a bacillus by Scheurlen, in 1887, however, until the careful work of Senger showed that this famous "cancer bacillus" was simply the well-known "potato bacillus" or Bacillus mesentericus fuscus. This upset the bacterial theory of the etiology of carcinoma; and although Kubassoff, in 1890, describes a new bacillus cultivated from cancer, and appearing, according to his researches, to fulfil all Koch's laws, a reaction of feeling had set in, and a new idea—namely, that protozoa were the cause of the disease—had met with more popular favor. The investigation of the protozoan theory led to the discovery that many different bacteria could be cultivated from carcinomata, but that they probably all entered from the skin, and were associated with the inflammatory, degenerative, and necrotic processes occurring in the tumors rather than with their etiology, and at the present time it is almost universally conceded that bacteria are of no significance.

Protozoa and Carcinoma, First Period.—Virchow observed cellular inclusions in carcinoma, and illustrated a paper which appeared in the first volume of his *Archives* with a beautiful plate showing them. He regarded them as examples of endogenous cell formation. Thoma, in a paper published in 1889, seems to have been the first to suggest that they were parasites. The same idea also occurred to Malassez, Albarran, and Darier in the same year. The stir that these opinions made was considerable, and many descriptions of the peculiar bodies were written within a year or two, all differing slightly as to the details, but only as might be accounted for by the different materials, different fixatives, and different staining-methods employed. Vincent, Wickham, Sjöbring, and others wrote in favor of their parasitic nature, some considering the bodies to be coccidia, others not attempting to classify them. Schütz, in 1890, doubted their parasitic nature, and described them as *pseudococcidia*, resulting either from cellular degenerations or from accidentally present red blood cells in the cells. L. Pfeiffer figured possibly parasitic bodies which he observed in cancers, but did not commit himself fully in regard to them. Heukelon, after a study of 200 tumors, could not convince himself that the bodies present were parasites; and Hauser could find nothing about those which he observed to prove them to be such.

In 1890 Russell discovered an entirely new object, which he described as the "fuchsin body" and regarded as a yeast plant. He suggested that it was the true parasitic organism, and so diverted investigation into an entirely new field. While the investigations were in progress, however, the protozoan advocates continued their work. Many papers appeared, but for a time (1890–92) the opinions expressed were almost equally divided. In 1892, however, several papers appeared by Podwyssozki, Sawtschenko, and Soudakewitch, the last supported by Metschnikoff, in which an attempt was made to trace the developmental and reproductive cycles of the supposed parasites. Ruffer and Walker, also supported by Metschnikoff, discovered a method of defining what appeared to be an intracellular parasite, for which a positive reproductive cycle seemed to be worked out. Delepine, however, in a critical survey of the then (1892) considerable literature, pointed out that though many observers had described parasite-like bodies, no one had yet proved them to be parasites, and summed up the situation as follows: "I, therefore, consider that even with the support of such an eminent authority as Metschnikoff, neither Soudakewitch nor Ruffer has any more right for the present to call the bodies to which they have attracted attention either protozoa or parasites than those who have described the same bodies previously." Plimmer (1892) confirmed the observations of Ruffer and Walker, while Karg (1892) argued against the parasitic theory. Clarke (1892) discovered what he supposed to be a form of conjugation of certain psorosperms in a carcinoma of the nose.

The protozoan theory reached its climax in the reported discovery by Korotneff of worm-like bodies which he named Rhophalocephalus carcinomatosis, supposed to be gregarinæ, in a case of squamous epithelioma, and in the extraordinary theory of Adamkiewicz that the carcinoma cells themselves were protozoan parasites.

From 1893 the papers supporting the protozoan theory seemed to diminish in number. Too many different forms had been described, scarcely any two writers agreeing concerning them, and no one having succeeded in proving the parasitic nature of any.

Blastomycetes and Carcinoma.—It was Russell who started this investigation by surmising that the "fuchsin bodies" he observed were yeasts. The bodies described by Sjöbring, and called by him "sporozoa," may have been yeasts. Roncali took great interest in the subject in 1895, and, in reviewing the work already done, thought the bodies described by Thoma, Sjöbring, and many of the other writers were probably yeasts. The investigations of yeasts were continued by Roncali and Sanfelice for some time, but nothing positive resulted from their work.

The greatest success was attained by Plimmer, who studied 1100 cancers and found the well-known bodies in almost every case, not only in the primary, but also in the metastatic, tumors. Though it is difficult to differentiate clearly between the bodies he found and those of a dozen of his predecessors, the objects have now pretty generally become known as "Plimmer bodies." One marked advance was made by these extended investigations, and that is the simplification of the subject, for instead of finding a variety of differing objects, Plimmer always found the same bodies, thus increasing the probability that they were definite and important entities. Plimmer also succeeded in cultivating some yeasts from cancers, but it is difficult to harmonize the appearances presented by these yeasts in culture with their appearances in the cancer cells, and it seems highly improbable that the two are identical. Further, the cultivated yeast, when inoculated into animals, produced nodules consisting chiefly of embryonal connective tissue, and in no way like carcinoma.

Revival of the Protozoan Theory.—The researches of Gaylord, under the direction of Park, have led to a revival of the protozoan theory in a slightly modified form. Gaylord accepts the Plimmer body as the probable parasite, but looks upon it as a protozoan parasite. He believes that it is an organism which in one stage of its existence circulates in the blood in the form of a minute sphere, and in another stage invades the epithelial cells. In the separated blood serum of carcinoma patients he has seen it increase in numbers upon prolonged incubation. The results of inoculation with this incubated serum containing many parasites are said to have produced a tumor resembling carcinoma in one out of many trials. The work is too new to be accepted at present.

From this review of the literature it will be evident that with the evolution of parasitology theories regarding the infectiousness of carcinoma have kept pace. When men were most interested in the study of bacteria, they found them in the tumors; when protozoa were shown to infect the epithelial cells of the lower animals, and their attention was turned to the sporozoa, they naturally looked for them in carcinoma; and when the blastomycetes were found to be of some importance, they were not slow to produce yeasts cultivated from the tumors.

All that can be said is that the parasitic nature of carcinoma is not proved. There are certain marked differences between tumors and other infectious processes. Thus, it is true of every known infection that the reaction induced by it is chiefly exerted upon the mesoblastic connective tissue. All productive infectious processes are characterized by proliferation of one tissue only—the fibrillar connective tissue. No matter in what organ they occur, the infectious agents affect the interstitial tissue chiefly, the other elements suffering atrophy and degeneration.

In carcinoma we find the epithelial cells essentially affected, and affected in such manner as to occasion proliferation, not degeneration. It is the epithelial cells that are at fault, and the fault is in their unlimited vegetation. It is the epithelial cells themselves that occasion the metastases, not the parasites, for in each metastatic tumor cells of recognizable type are found, and the metastasis of gastric carcinoma, pancreatic carcinoma, mammary carcinoma, and squamous epithelial carcinoma can very often be differentiated with the greatest readiness by microscopic study.

Almost without exception the active infectious processes are transmissible upon inoculation, but thus far the inoculation experiments with carcinoma are almost without fruition.

ADENOMA.

An adenoma is a tumor whose structure resembles that of an epithelial gland. Like a gland, it consists of acini, ducts, and supporting vascular connective tissue. Unlike a gland, it is usually so constructed that utility is precluded because of a marked disproportion of the component elements, acinose and canalicular, and an absence of proper outlets. The tumor, being typical in structure, is benign.

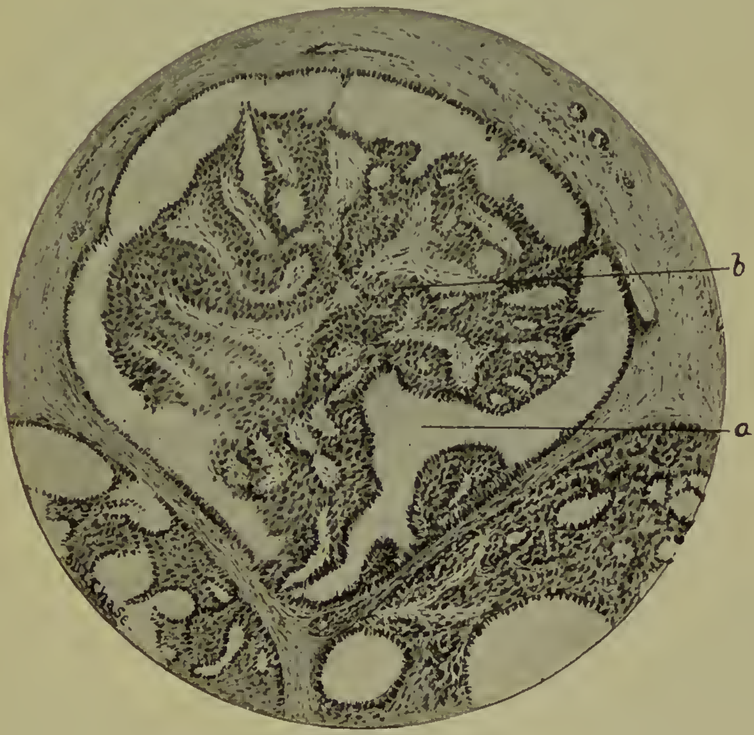

FIG. 116.—Adenocystoma papilliferum of the mammary gland: *a*, Dilated duct; *b*, papillary outgrowth from the epithelial lining. Tumors of this structure are commonly malignant.

Seat of Occurrence.—Adenomata always grow from epithelial glands, and any such organ may form their starting-point. They have been observed in the mammary gland, ovary, liver, kidney, thyroid, adrenal, salivary, lacrimal, sebaceous, and sweat glands, and have also been observed to arise from the tubular glands of the mucous membranes. They are most frequent in the mammary glands.

Special Forms.—Cystic adenomata are sometimes called *adenocystomata* or *adenoceles*. When such tumors contain papillæ growing into the ducts, they form the *adenocystoma papilliferum.* The alveolar and canalicular, simple and fibrous, forms have already been fully described. The fibroadenomata of the mammary gland are described under the tumors of that organ. (See Tumors of the Mammary Gland.)

One of the most frequent forms is known as the *adenomatous* polyp. It occurs upon the mucous membrane of the nose, pharynx, larynx, stomach, and intestine, and consists of fibroconnective tissue, usually in an advanced state of myxomatous degeneration, with glandular tubules ramifying through it. These polypi may be as small as peas or as large as walnuts.

The adenoma of the thyroid is sometimes called a *bronchocele*, that of the ovary, a *multilocular cyst.* The last mentioned are the largest of the adenomata, sometimes containing so many and such enormous cysts as to hold many gallons of fluid and weigh 100 pounds. The greater number of adenomata do not attain any considerable size or produce any important symptoms.

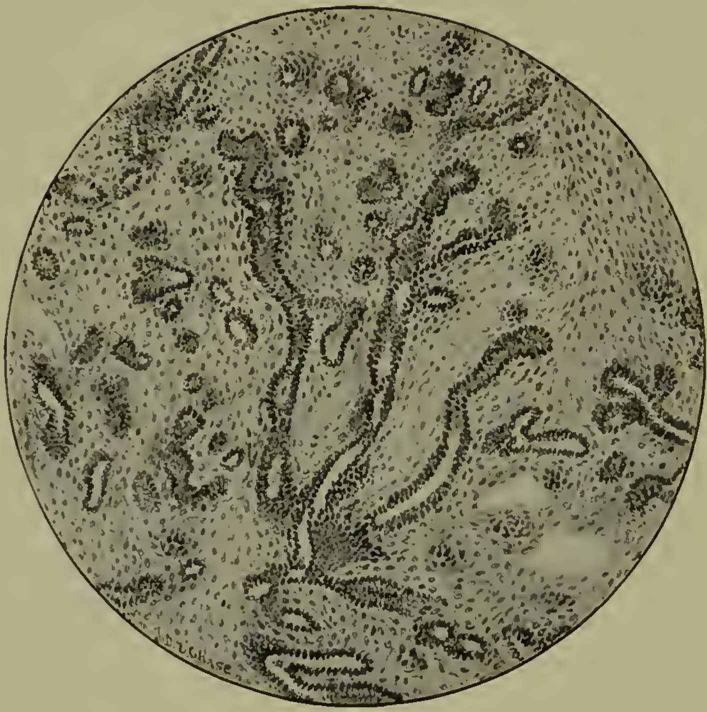

FIG. 117.—Fibro-adenoma of the mammary gland (canalicular form). Oc. 2; ob. 3.

An interesting tumor of the adenomatous type occasionally occurs in the kidney and is known as *hypernephroma.* It is supposed to depend upon the inclusion of fragments of the adrenal substance in the kidney tissue. Aberrant adrenal fragments are not infrequent in the abdominal cavity, and sometimes are as far removed from their normal position as to be found in the pelvis. The subsequent growth of such fragments may lead to the formation of a tumor in or upon the kidney, with all the structural characteristics of the adrenal gland, the cells containing both fat and glycogen. Many adenomata of the kidney supposed to originate from the uriniferous tubules have, no doubt, had this origin.

Morbid Anatomy.—Nearly all adenomata are well circumscribed and encapsulated, and are thus differentiated from the surrounding tissue, though almost without exception homologous tumors, resembling the tissue of the gland in which they grow. They usually possess a rounded or nodular form, and are apt, in consequence of their shape, to form projecting elevations, which, while usually sessile, may be pedunculated, and in the case of such growths as form upon the mucous membranes of the nose, larynx, stomach, and intestine, even become polypoid.

Morbid growths sometimes incorrectly called adenoma consist of uncircumscribed hyperplasiæ of glandular tissue. Some term these *diffuse*, others *malignant, adenomata*, but it is probable that they are simple glandular hyperplasiæ when benign, or carcinomata when malignant. The duct hyperplasia that accompanies cirrhosis of the liver, and the glandular proliferation of the endometrium (glandular endometritis) and of the cervix uteri, are of this class and cannot correctly be classified as adenomata.

Pathologic Histology.—As has been shown, the tumor consists of a vascular fibrous stroma, which shows a marked tendency to myxomatous degeneration, and a varying proportion of glandular tissue. When the proportion corresponds with that of the normal gland, the tumor is called a *simple adenoma*. If, however, the amount of glandular tissue be very inconsiderable, it is called a *fibro-adenoma*.

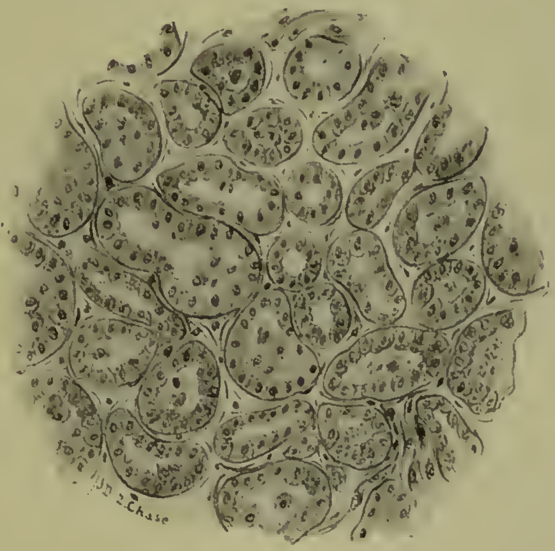

FIG. 118.—Alveolar adenoma of the mammary gland. Leitz, Oc. 2; ob. 9.

The predominance of alveolar or canalicular elements makes the tumors easily divisible into *alveolar*, *racemose*, or *acinose adenoma* and *canalicular* or *tubular* varieties.

The simple alveolar adenoma most closely repeats the structure of the gland; the canalicular fibro-adenoma, least so.

The cells for the most part resemble in size, form, and arrangement the normal gland, though they may be more or less crowded and in double or even triple layers. A normal relation of the cells to the basement membrane is the essential microscopic feature of adenoma, and it makes little difference whether glandular or fibrous tissue, or alveolar or canalicular tissue, predominates, so long as the disposition of the cells is normal and their relation to the membrana propria shows that they have no disposition to invade the matrix. It is this difference which separates adenoma from carcinoma.

Racemose or alveolar adenomata occur only in connection with the racemose glands—*i. e.*, the mammæ, salivary glands, etc. From the ducts of the same glands tubular or canalicular adenomata may also occur.

When incised, the contents of the tumor are usually observed to be under pressure, and, after having been separated, the halves cannot again be accurately approximated, the surfaces at once becoming convex. The cut surface resembles the gland in which the tumor occurs. Thus, in the mammary gland it appears grayish or pinkish white and has its substance divided up into minute lobules by the intermediate connective tissue, which in rare cases contains fat. In the thyroid gland the color is reddish or orange and appears purely glandular.

The tumors are not infrequently cystic, and in the adenoma of the ovary the cysts become the conspicuous feature, and the growth is so frequently spoken of as a *cystoma* that one is apt to lose sight of its true nature.

The capsule consists of connective tissue, usually well differentiated from that of the surrounding gland, so that the surgeon often "shells out" the tumors readily. Occasionally, however, the enucleation is less easy, and the connective tissue of the tumor and gland seems to be continuous. Such cases are spoken of as "adherent capsule," and are looked upon with suspicion as to their disposition, it being supposed that if the connective tissue of the gland and tumor is continuous, the epithelial elements are probably also continuous, and the recurrence of the growth more liable to occur than when it is free.

The matrix of the adenoma consists of fibroconnective tissue with elastic fibers, and is prone to myxomatous change. The cells of the tumor, being the offspring of functional glandular cells, inherit in part their function, and discharge more or less atypical secretion into the ducts. From these it may be expressed in the form of creamy matter when the tumor is incised. It is this secretion which, in large quantity, fills and causes distention of the ducts and acini which form the numerous cysts. The contents of the cysts resemble the glandular secretion—colloid substance in the thyroid, milk in the mamma, bile in the liver, water, colloid, or pseudomucin in the ovary, etc.

In some adenomata, especially those of the mammary gland and ovary, papillary outgrowths (papillomata) from the walls of the ducts and cysts project into and dilate them. Such a formation is spoken of as an *adenocystoma papilliferum.* This may occur in innocent tumors, though it seems to indicate a vegetative activity that commonly results in a change in the tendency and disposition of the tumor. Such a growth may occur in a single cyst, or every duct throughout the tumor may be lined with the little papillary excrescences.

The tubular adenomata, apart from those originating from the ducts of the racemose glands, also arise from the tubular glands themselves, and occur in the cervix uteri, kidney, liver, sweat glands, and other tubular glands.

Disposition.—The adenoma is a thoroughly benign growth, and so long as it conforms to the typical structure will not recur after excision, give metastasis to other organs, or occasion any inconvenience other than may result from pressure. This, naturally, may be serious in the case of the large ovarian tumors mentioned.

Termination.—The tumors grow until natural causes, such as the failure of nourishment by leading to retrogressive changes, checks them. They then remain stationary or grow very slowly and may last indefinitely. Spontaneous improvement has sometimes been observed in mammary tumors, but can be attributed to the absorption of fluid from contained cysts or some other simple mechanical accident rather than to any disappearance of tumor tissue.

ODONTOMA.

An odontoma is a tumor-like enlargement resulting from malformation of a developing tooth. Such perversion of development may occur before the tooth has begun to form and result in a tumor-growth of the germ, or may occur after the tooth has fully formed, or at any intermediate period. The structures entering into the formation of the odontomata may be derived from the enamel organ (epiblastic) or from the dentin or cementum (mesoblastic).

Sutton, in his splendid description of these tumors, finds it convenient to describe seven different forms :

From the enamel organ	epithelial odontoma.
From the tooth-follicle	follicular odontoma. fibrous odontoma. cementoma. compound follicular odontoma.
From the papule	radicular odontoma.
From the whole germ	composite odontoma.

1. The **epithelial odontoma** develops from the enamel organ and forms more frequently in the lower than in the upper jaw. It usually occurs in young adults and forms a large tumor, which may attain the size of a small hen's-egg. Upon examination it is found to be fairly well encapsulated and made up of a congeries of cysts of various shapes and sizes, separated by thin walls, sometimes partly ossified. Growing parts of the tumor are said to have a reddish color not unlike myeloid sarcoma.

Microscopic examination shows the epithelial elements derived from the enamel organ to form a mass of branched anastomosing columns of epithelium forming alveoli, which bear a partial resemblance to adenoma. The cells lining the alveoli are, however, of several layers, the outer layer consisting of columnar cells, while the central cells degenerate and give rise to tissue resembling the stratum intermedium of the enamel organ.

2. **Follicular odontomata** or **dentigerous cysts** consist of tooth follicles whose pathologically thickened walls have resisted the eruption of the tooth, which is retained in a cavity or cyst formed by dilatation of the follicle by viscid fluid. The tooth is sometimes deformed to the extent of having truncated roots. The walls of the cyst usually contain calcareous or osseous tissue. The cysts rarely suppurate.

3. **Fibrous odontoma** depends upon a great thickening of the connective-tissue capsule surrounding the tooth and blending with the dentin papilla, by which the tooth is so surrounded by laminated fibroconnective tissue that it is unable to be erupted. Calcareous matter may be deposited between the lamina of this connective tissue. Sutton found this form of odontoma especially frequent in goats; they also occur in man. Sometimes they are multiple and they may be symmetric.

4. **Cementoma.**—Sutton regards the cementoma as depending upon ossification of thickened capsules, such as constitute fibrous odontoma. By this means the tooth becomes surrounded by a mass of cementum. The tumor occurs in man, but is particularly frequent in horses. It may attain a large size, and Sutton has described one that weighed 25 oz., and consisted of three teeth embedded in a mass of cementum. The largest on record, preserved in the Royal Veterinary College of London, weighed 70 oz.

5. **Compound Follicular Odontoma.**—Sutton looks upon this tumor as depending upon the sporadic ossification of the thickened capsule, by which a number of small teeth or denticles consisting of cementum or dentin, or

even ill-shaped teeth composed of three dental elements—cementum, dentin, and enamel. The number of such denticles contained in such a compound follicular odontoma may reach 400. Such tumors occur in man, and also in the lower animals, as the goat and horse.

6. **Radicular Odontomata.**—These tumors arise after the crown of the tooth has been completed and while the roots are in process of formation. They form elongated, pyriform, or irregular outgrowths from the roots of the teeth, and may be many times as large as the tooth itself. The growths consist of both dentin and cementum, the cementum forming the outer layer.

Radicular odontomata occur in man and the lower animals. Sutton has observed them in rodents in particular because of the persistent pulps from which their teeth grow. The largest odontomata known are radicular odontomata growing upon the tusks of elephants.

In discussing these growths Burchard inclines to the opinion that they are the result of hernial projections of the pulp of the tooth.

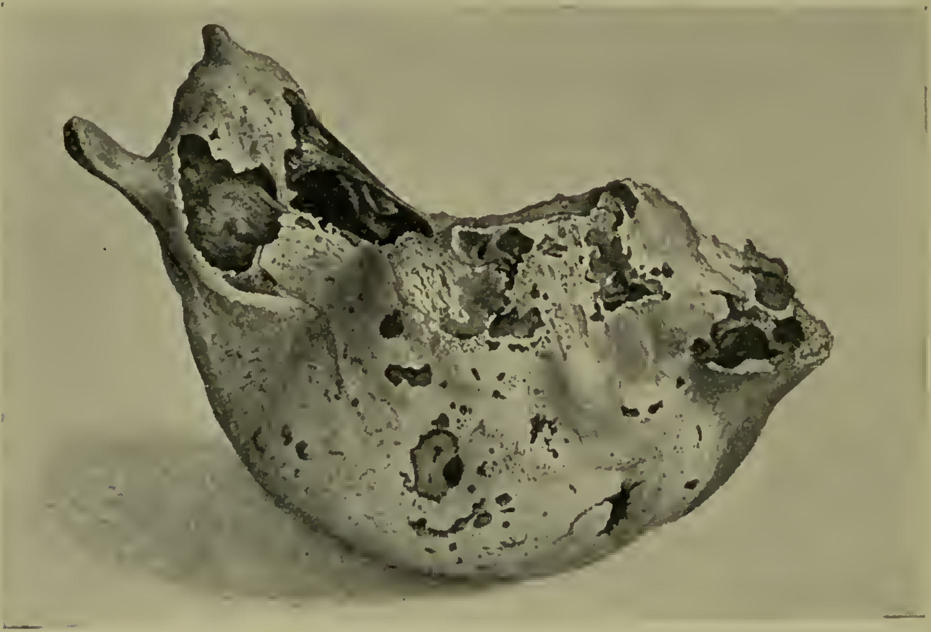

FIG. 119.—Cystic tumor of the jaw, probably dentigerous (Warren Museum).

7. **Composite Odontoma.**—Sutton gives this as a convenient term by which to describe all the hard tooth tumors which bear little or no resemblance in shape to teeth, but occur in the jaws and consist of a disordered conglomeration of enamel, dentin, and cementum. Such odontomata may be considered as arising from an abnormal growth of all the elements of a tooth germ—enamel organ, papilla, and follicle.

The tumors are not uncommonly composed of two or more tooth germs fused together. This form of tumor appears to occur in human beings only. They may attain a considerable size : one of the largest on record, removed by M. Michou, weighed 1080 gr. ; the largest removed by Hilton, of Guy's Hospital, weighed 15 oz.

They frequently grow into the antrum, and no doubt many exostoses of the antrum are of this nature. They often suppurate and give rise to symptoms which make possible the erroneous diagnosis of necrosis. Most of the well-known tumors have been removed surgically, but a few have spontaneously separated after suppuration and ulceration of the surrounding parts.

Their irregular shape, hardness, whiteness, and the occasional appearance of what correspond to cusps on the surface are usually sufficient to enable the diagnosis to be made.

TERATOID TUMORS.

Cholesteatoma.—The cholesteatoma is a peculiar and rare tumor, characterized by the formation of pearly bodies, consisting of scale-like epithelial cells with occasional admixture of cholesterin.

It seems that at present several quite different formations are included under this genus, and it is doubtful what their histogenesis really is, some regarding the cells of which they consist as endothelial cells, though the majority believe them to be epithelial.

Seat of Occurrence.—Cholesteatomata occur in the pia mater, choroid plexuses, tuber cinereum, and other parts of the brain, and very rarely in the spinal cord. Another species or variety of the tumor occurs in the cavity of the middle ear, while still another variety sometimes occurs in the urinary passages.

1. The *cholesteatoma of the nervous system* is in all probability a teratoid or monstrous growth, which Boström explains by assuming that in the early development of the embryo, at the time of the closure of the medullary canal, of the constriction of the secondary anterior cerebral vesicle, of the anterior or middle cerebral vesicle, or of the middle and posterior vesicles, about the fourth or fifth week of embryonal life, epidermal cells are caught in the pia mater.

The tumors are subsequently observed as small, smooth, occasionally nodular growths, of rather soft consistence and smooth, shining appearance. They may be as large as a pigeon's egg.

Microscopic examination shows the tumors to consist of an areolar tissue in which are numerous rounded bodies, bearing marked resemblance to the "pearls" of epithelioma. These are formed of concentrically arranged flattened epithelial cells. Plates of cholesterin are sometimes contained within them, and hairs have occasionally been found in the tumors, thus proving their epithelial and epiblastic origin.

The growths are usually discovered where their presence was not suspected, and are entirely benign. Pressure upon the brain may cause symptoms.

2. The *cholesteatoma of the middle ear* sometimes occurs in the antrum, mastoideum, and meatus. It may reach the size of a cherry, or even of a hen's egg, and has a whitish color, sometimes with a tinge of blue or yellow.

The mass is built up, like an onion, of concentric layers, and consists entirely of cornified epithelium which has gained entrance into the middle ear through openings in the drum. The presence of the increasing masses may cause the disappearance of the normal cylindric epithelium of the part, and by pressure may even lead to atrophy of the bones. It is possible that in some cases the epithelial cells may not have entered from without, but may have formed in the tympanic cavity from cells originally included there in embryonal development.

3. The *cholesteatoma of the urinary passages* is a rare formation resulting from chronic inflammation and characterized by keratosis of the epithelial cells. Ziegler, by whom it is mentioned, gives no particulars regarding its appearance.

Dermoid Tumors or Cysts.—A dermoid tumor is a peculiar teratoid formation, usually cystic in nature, and characterized by the presence of tissues derived from all three blastodermic layers. It is called dermoid because of a preponderance of the epiblastic formations, especially skin and its appendages, hairs, sebaceous and sweat glands, and teeth. Bone, cartilage, glands, etc., are also present.

Although occasional instances of the occurrence of dermoid tumors are mentioned in the early writings, very little attention seems to have been devoted to them until Blumenbach (1785) rejected the then popular belief that they were punishments inflicted by God upon those who had been guilty of moral errors, and suggested that their formation was due to a definite *nisus formativus*. Baillie further refuted the old idea by the discovery of an ovarian dermoid containing skin, hair, and bone in a little girl (a virgin) twelve years old. From the study of this case Baillie was led to conclude that the genital organs of the human female were able in themselves, without fertilization, to generate and develop an embryo. A few years later Tumiati wrote upon dermoids, and regarded their formation as analogous to that of the double monsters. Still later Meckel, in an interesting paper, concluded that they originate from (1) conditions akin to pregnancy; (2) double monsters; and (3) the change of normal tissue into tissue of another kind in consequence of irritation. In 1854 Remak further changed the views concerning them by showing that they were frequently congenital and occurred at positions in which fetal clefts, fissures, or sinuses previously existed.

Seat of Occurrence.—Before the time of Remak's paper it was remarked that dermoid tumors occurred in the ovary and orbit with great frequency, but that certain parts of the body were seats of predilection does not seem to have been observed. Remak observed that they occurred by preference at positions in which the union of fetal clefts, fissures, or sinuses took place, and at which elements from the skin could be sequestrated.

This is in great part true. We find them occurring in the great median fissures of the body, both anteriorly and posteriorly; in the mandibular fissure, orbital and naso-orbital fissure, branchial clefts, in connection with the sutures of the brain case, and nasopharynx. The fact, however, that they occur with great frequency in the ovary, occasionally in the testicle, and frequently in the abdominal and thoracic organs, is opposed to the theory of Remak. The ovary is the most frequent seat of occurrence. They have, however, been found in the pituitary body (Beck), in the olfactory bulb (Bonorden), in the esophagus (Hess), arch of the aorta (Stilling), lower lobe of the left lung (Coelta), apex of the right lung (Salmonsen), and in the anterior surface of the heart (Pindus).

Meckel discovered a dermoid tumor of the diaphragm from which 21 fragments of bone, 4 teeth, and considerable hair were removed. Ruysch found one in the omentum, Andral one in the mesentery, and Fränkel one in the peritoneum. Bonfigli described one which was adherent to the liver and stomach through an intermediate band; it contained teeth. Modelung described one from the kidney.

Ovarian dermoids are common. Olshausen found that of 2275 ovarian tumors, 80—*i. e.*, 4 per cent.—were dermoids. They are more common on the right side than on the left. Mantel observed 191 cases, and found that 97 were on the right side, 67 on the left, and 26 double-sided.

Pathologic Anatomy.—The tumors appear to begin as solid growths, and subsequently become cystic by the retention of sebaceous matter, the secretion of sweat glands, and the accumulation of exfoliated epithelium. They may be congenital and develop rapidly after birth, or they may develop late in life. It is known that dermoids of the ovary have occurred in organs examined at operations prior to their formation and found to all appearances healthy. They form more or less rounded, smooth, occasionally very adherent tumors, which vary in size from a pea to a man's head or even larger. They usually have a putty-like consistence from the large quantity of fatty sebaceous substance they contain. In the ovary they cause much pain. Tissues of all these blastodermic layers are present.

Epiblastic Elements.—The *skin*, when present, does not cover the entire interior of the cyst, but occurs in more or less elevated patches, velvety in appearance, scattered upon the cyst wall. The skin patches are usually, sometimes excessively, supplied with villi, and the skin is generally furnished with an excessive number of large sebaceous glands.

Sweat-glands occur, but are less common.

Typical *hair follicles* are usually present, and form hairs which are generally soft and downy, but sometimes long and coarse. The hairs are usually blond, but may be brown or even black, and are always similar to those normal to the animal. In the negro the hairs are flattened and curly; in sheep I have found small dermoids filled with soft wool; in the hog it is said that bristles occur, and Sutton states that the dermoids of birds contain feathers.

Occasionally the skin covers smooth, rounded eminences suggesting *mammary glands*, and even provided with *nipple-like projections*. According to Sutton, these gland-like bodies are generally fatty in structure, but may be real mammary glands, provided with ducts passing through the nipple, and secreting colostrum.

Horns and *warts* also occasionally occur in dermoid cysts.

Cerebral tissue may occur in dermoid tumors, especially if they contain bone, and not infrequently scattered nerve cells, resembling the motor nerve cells of the spinal cord, as well as nerve fibers, are found.

Teeth of various shapes—incisors, canines, and premolars—occur. In the tumors which I have examined the teeth were without roots and resembled the milk teeth rather than the permanent teeth. They are usually well formed and white; sometimes deformed and discolored.

Parts of the cyst wall not covered with skin are usually covered with a mucous membrane with either squamous or columnar epithelium. The columnar epithelium is sometimes ciliated. In this mucous membrane *mucous glands* may be present.

The cyst is generally full of a greasy granular material, in which are scattered teeth, hair, epithelial cells and pearls, sebaceous matter, cholesterin, and aqueous fluid probably derived from the sweat.

Mesoblastic Elements.—We read much about the epiblastic derivatives in dermoids, but it is only within a recent period that attention has been paid to the derivatives of the mesoblast and hypoblast likewise represented. *Bone* is commonly observed in the form either of spicules or of flattened plates.

Beneath the skin *bone* is not infrequently present in the form of flattened plates of irregular shape. Sometimes the bone is mandibular and contains sockets, from which teeth project through the epithelial covering into the cavity.

Cartilage is also met with, not, however, as antecedent to bone, for the dermoid bones are usually membranous in origin. *Striped* and *unstriped muscular tissue* and much *areolar tissue* are also common, and are, of course, mesoblastic in origin.

Hypoblastic Elements.—The hypoblast is probably represented by the columnar and sometimes ciliated epithelium and mucous glands.

Etiology.—Remak's theory that dermoids are sequestration tumors explains some, but not all, cases. What are known to us as dermoid tumors are undoubtedly several different, yet similar, things. The old writers saw no difference between dermoid tumors and ectopic pregnancies, inasmuch as what were regarded as fetal elements were discovered in them. This led them to the supposition that all were cases of imperfect conception, a theory which might readily apply to a dermoid of the ovary, but could hardly be applicable to one of the orbit. Such tumors gradually came to be regarded as cases of *inclusio fœtus in fœtu*, analogous to the double monsters. It is probable that there is truth in both these theories. Some tumors are certainly formed by the sequestration of fetal tissue during the arching-over processes of embryonal development, tumors of this kind being described as *sequestration dermoids*, and occurring in the neighborhood of the fissures, as has already been pointed out. Others are cases of *inclusio fœtus in fœtu*. The ovarian and testicular dermoids must, however, be otherwise explained, as they can be acquired late in life.

Theory of Parthenogenesis.—Wilms doubts the congenital origin of the ovarian and testicular dermoid tumors, and in speaking of the theories thus far mentioned, says that it serves to complicate matters rather than to elucidate them.

If the tumors are not congenital, they must, of course, be developed in after-life, and we must look into the tissues in which they occur for the cells from which they can originate. Sutton suggests that the epithelial cells of the *membrana granulosum* are endowed with great vitality, and are responsible for the development of the tumors and their contents. Wilms is, however, of a different opinion, and sees in the ovum itself a cell capable of producing tissues of all kinds when fertilized. For the elaboration of his theory he brings forward the developmental cycle of the ovum itself, and calls particular attention to the extrusion of the polar granules. These are regarded as a kind of male element in the female cell, which must be extended before the ovum can be ready for fertilization. If the powers of extrusion miscarry and the granules remain within the ovum, Wilms believes that parthenogenesis can take place and an atypical and monstrous development of the ovum result in the production of a dermoid tumor instead of a fetus. He supports his view by observations upon 19 cases of ovarian dermoid tumors, all of which were subjected to a careful microscopic study. In each of them tissue derivatives of all three layers of the embryo were found—skin with hair, sebaceous glands, sweat glands, and teeth representing the epiblast; blood vessels, striped and unstriped muscle, and bone representing the mesoblast; and columnar ciliated epithelium in a rudimentary tube or sac, supposed to be the hypoblast. So satisfied is Wilms that the ovarian dermoids originate in this way that he suggests abandoning the term dermoid, with the misconceptions attached to it, and calling the growths "*rudimentary ovarian parasites*" instead.

Nature and Disposition.—Dermoid tumors are benign in nature, although their growth in some locations is accompanied by pain. A few rare cases are on record in which the epithelial tissues in the tumors took on a carcinomatous development. The combination of dermoid and adenoma also occurs. Although benign, a case of apparent metastasis is reported by Emanuel, who observed a dermoid tumor in the rectus muscle after removal of an ovarian dermoid.

Kollaczek has also reported a most extraordinary case of richly disseminated epithelial clumps over the entire peritoneum. In the center of each nodule a hair was visible. Fränkel has seen a somewhat similar case.

The rupture of an ovarian dermoid and of other dermoids is always a serious matter, because of the irritating foreign matter which escapes into the peritoneum, and because of the danger of disseminated tumors.

The **diagnosis** of the dermoid tumors is not always possible before removal, and sometimes difficult afterward, especially if hair, teeth, bone, and other easily recognized characteristics are absent. The contents of the cyst are, however, usually characteristic, for scarcely any other lesion furnishes the smeary, turbid material which can be evacuated from a dermoid tumor. Examination of the cyst wall by the microscope generally makes the condition plain by revealing epithelium and its appendages.

It may be very difficult to differentiate between a dermoid tumor and an ectopic pregnancy. Wilms points out that this should offer few difficulties to the microscope, because of the invariable presence in ectopics, and invariable absence in dermoids, of placental or decidual tissues.

CYSTS.

A cyst is a well-circumscribed, pathologic collection of fluid, tending to persist and increase. The word is employed so loosely that it is difficult to define it accurately. By some writers inflammatory formations would be excluded immediately, yet by the greater number exudations into bursa, the tunica vaginalis testis, etc., are included. Large collections, such as occur in the peritoneal cavity in ascites, are rarely called cysts, though their formation and structure are identical with those of the bursa and hydrocele. Abscesses are to be excluded because of their distinctly inflammatory origin.

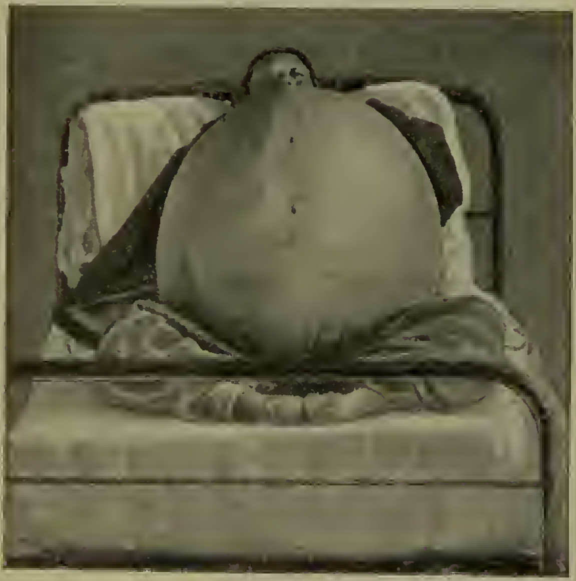

FIG. 120.—Large ovarian cyst in a Chinese woman (Reifsnyder).

A cyst may or may not be provided with a circumscribing wall, depending upon the mode of its formation. The greater number are lined by a membrane supporting either epithelium or endothelium, so that their structure is distinctly vesicular.

Cysts may occur singly or in groups, the latter being known as *multilocular* cysts. A morbid growth containing a number of cysts, by softening, is described as *cystic*. A tumor formed of epithelial alveoli enclosed in a fibrous matrix whose alveoli have a marked tendency to become cystic is called a *cystoma*.

The following varieties may be described: 1. Retention cysts. 2. Exudation cysts. 3. Colliquation cysts. 4. Parasitic cysts. 5. Dermoid cysts.

1. **Retention Cysts.**—These are caused in consequence of pathologic obstruction to the ducts or tubules of glands, which are dilated by the retained secretions.

Retention cysts are common in the skin from obstruction of the outlets of the sebaceous glands, forming *comedones*, and *atheroma* or *wen*, and from obstruction of the sweat glands, forming *milium*. They are frequently observed upon the mucous membranes of the respiratory, digestive, and genito-urinary tracts. One of the best known is the *ovula* or *follicle of Naboth* (Nabothian follicle) of the uterine glands. Cysts of the kidney, such as occur in chronic interstitial nephritis, are also familiar examples. *Galactoceles*, from retention of milk in the mammary gland; *spermatoceles*, from retention of sperm in the testicles; *ranula*, from obstruction of the parotid duct, will also suggest themselves as good examples. Similar formations also occur in the pancreas and liver. Larger cysts occur from obstruction of the Fallopian tubes (*hydrosalpinx*), appendix vermiformis, ureters (*hydronephrosis*), and gall-bladder.

Retention cysts increase in size by the continuous accumulation of their contents until their walls become so attenuated as to yield to accidental pressure and rupture. As they increase they push aside the surrounding structures and, following the direction of least resistance, find their way to the surface of the organ, from which they eventually project. The contents of such a cyst correspond originally with the secretion of the gland, but as time goes on the retained fluid becomes gradually changed and more and more aqueous. Even in the gall-bladder with its viscid bile a permanent obstruction is apt to be followed by a transformation of the contents, which ultimately results in a collection of a clear watery fluid. Occasionally, for reasons not clear, the fluid in a cyst is absorbed, leaving the shrunken cavity with a small amount of solid contents, evidently the sediment from the previously present fluid.

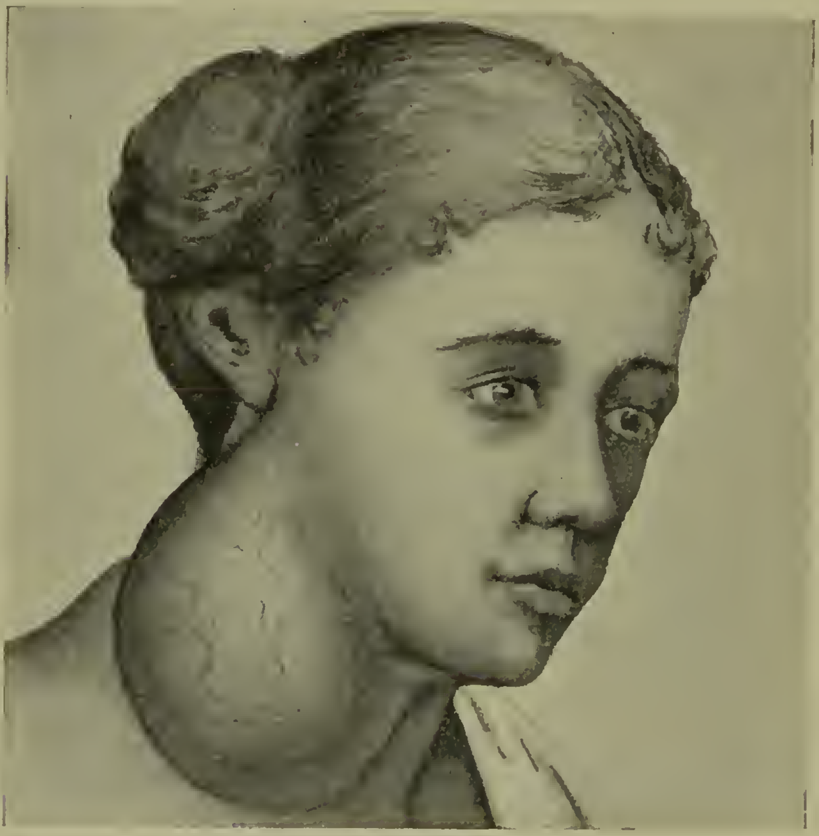

FIG. 121.—Branchial cyst (Gould).

Cysts sometimes form by the dilatation of the alveoli of ductless epithelial glands, in consequence either of overproduction or of diminished absorption of the contents. It is doubtful whether such cysts, occurring in the thyroid, pituitary, and adrenals (?), should be called retention cysts or whether they should be included in the next class.

2. **Exudation Cysts.**—These are formed through the accumulation of fluid in spaces naturally without outlets. They are for the most part endothelial-lined serous spaces. Such cysts develop from irritated bursæ and form "*housemaid's knee*," *bunions*, *ganglia*, etc. Such collections may also occur in the tunica vaginalis testis and lead to *hydrocele*.

Exudation of fluid into remnants or vestiges of fetal structures sometimes occasion the formation of what Sutton has described as *tubulocysts*. These structures are chiefly epithelial in character, but are naturally closed and out of service, and exist solely because of the failure of their natural involution. Such cysts occur from vestiges of the urachus, parovarium (Wolffian tubules), vagina (Gärtner's ducts), branchial clefts, thyrolingual duct, omphalomesenteric duct, postanal gut, etc. They may be insignificant in size, or, as in Ferguson's case of cyst of the urachus, may contain several liters of aqueous fluid.

3. **Colliquation cysts** result from softening of solid tissues by retrograde or necrotic processes. Such cysts commonly form in neoplasms from myxomatous degeneration, and also occur in the central nervous system after hemorrhage, thrombosis, and embolism, with softening of the nervous tissue. Colliquation cysts, in consequence of their mode of formation, are irregular in size and shape, without lining membranes, and have varying contents. A tumor may be honeycombed throughout with cysts of this formation. The older the cyst, the more fluid the contents will be, and the more aqueous the fluid will appear. Mucus, pseudomucin, and colloid material commonly occur in such cysts in tumors ; clear aqueous material, sometimes with crystals of hematoidin, in such cysts in the brain. If formed by fatty metamorphosis of the tissue, the contents may be fatty.

4. **Parasitic Cysts.**—In rare instances parasites may lodge within the ducts of glands and so occasion retention cysts. More frequently the cysts in which parasites are contained are the result of a reactive inflammation occurring in consequence of their presence in the tissues. Such cysts surround the trichina as it lies encysted in the muscles, and about the embryo tape-worms forming the Cysticercus cellulosa. Still more rarely the parasite itself may form the wall of the cyst, either with or without an additional support of hyperplastic connective tissue. This form of cyst, with daughter cysts within it, is seen in the human developmental stage of the Tænia echinococcus.

The wall of the echinococcus is bluish white, laminated, brittle, and has a marked tendency to reverse itself and roll up when torn.

In addition to the parasites, or such remains of them as their hooklets when the parasites are dead, the parasitic cysts usually contain clear aqueous fluid. When the parasites are dead and the contents of the cysts begin to be absorbed, they frequently calcify.

5. **Dermoid Cysts.**—These peculiar formations, sometimes solid, sometimes cystic, have already been fully described under the Teratoid Tumors (*q. v.*).

CHAPTER VIII.

PARASITISM.

Parasitism is a peculiar form of vital association which certain living beings assume toward one another, in which one called a *parasite* lives upon or within and at the expense of another called the *host*. As the parasite lives upon or within the host, it must be the smaller of the two. In its broadest sense parasitism is difficult to define, as it may be made to apply to birds depositing their eggs in other birds' nests, or to bees that take up their abode in others' hives, and to many departures from normal independent existence.

A parasite, in consequence of the acquired habit of life, may lose the power of independent life, so that it must die with the host or shortly after.

Every degree of parasitism can be found, from the pulex that lives in the cracks of the bedstead or wall and sallies forth at night to prey upon his sleeping host,—an example of a doubtfully parasitic existence,—the body-louse that lives in the seams of the clothing and preys upon the occupant, the head-louse that lives in the hair, etc., to the tape-worm that lives in the intestine devoid of sense-organs, of alimentary organs, and of circulatory organs.

Parasites, such as the insect forms described, are in a sense *optional* parasites, though their mouth-parts are so constructed that they cannot nourish themselves except by the sucking of blood ; parasites, such as the tape-worms, are *obligatory* parasites, because they cannot exist except in the one environment.

The ubiquitous distribution of the bacteria and the facility with which they can live everywhere make it somewhat difficult to say in how many cases they are truly parasitic when found in the higher organisms. Certainly all those varieties that live with difficulty apart from the parasitic conditions may justly be termed parasites.

Parasitism, especially among the bacteria, is frequently an accident of association—*i. e.*, the organisms are fitted for life under all ordinary conditions. On the other hand, among the higher forms, it is a habitual mode of existence, and the parasite may either have surrendered important vital organs rendered useless by its new mode of life, or may have had its mode of reproduction modified in order to insure progeny under the difficult and complicated conditions of its new life. Thus, the tape-worm needs no circulatory, alimentary, or sense organs, but to insure permanence of its kind produces an enormous number of eggs, very few of which are destined to find their way into the appropriate hosts for further development, and the filarial worms and malarial parasites must form an immense number of embryos before the occasional nocturnal mosquito of the appropriate species happens to take them up with the blood of its victim and afford a proper opportunity for sexual development.

Parasitism is responsible for a large number of diseased conditions to which attention must be devoted. The subject is, however, so extensive that its thorough consideration with a satisfactory description of the parasites would require a whole volume in itself, and only an introduction to the subject can be given in this work.

Both animal and vegetable forms of life, upon occasion, take up their residence in or upon the human body and derive their nourishment at its expense, occasioning inconvenience and disease, sometimes so trivial as to pass unnoticed; sometimes so serious as to destroy life.

The parasitic diseases are specific in that they have definite or specific causes; and infectious, in that their causes may be transferred from one individual to another. All infectious diseases depend upon parasites.

VEGETABLE PARASITES.

Fungi.—Plants of low organization, destitute of chlorophyl (except in rare cases), and deriving their nourishment wholly or almost wholly from organic compounds. This order includes the mushrooms, puff-balls, moulds, mildews, yeasts, and bacteria.

The vegetable parasites belong to the lowest fungi, and are without exception micro-organisms. They include the basidiomycetes (favus and thrush fungi), the mycomycetes (the common moulds), the phycomycetes (the mucor moulds), the saccharomycetes (a few yeasts), and the schizomycetes (bacteria).

Basidiomycetes.—Spores borne upon basidia.

Basidiomycetes.—*Achorion Schoenleinii*, the fungus of *favus* or *tinea favosa*. This organism, described by Schoenlein in 1839, is the cause of favus in man, in the domestic animals, and in some birds. Grawitz seems to have been the first to cultivate it artificially, though Kral improved upon his methods. He pulverized the favus crusts in a mortar with silica previously heated to incandescence, and from the finely divided material thus secured melted agar tubes were inoculated and plates prepared, upon which colonies developed from single scattered conidia.

Kral found that the organism grew at both the room and the body temperature upon agar, glycerin agar, blood serum, gelatin, bouillon, milk, malt infusion, eggs, potatoes, and beets. The growth was slow, requiring three or four days, and showed a marked preference for development beneath the surface of the media. Only upon potato and beet was there an exception to this rule, and then the surface growth is described as a loop-like or gallery-like layer perpendicular to the culture medium. There are characteristic moss-like projections from the growth, which extend outward and dip into the medium. The color of the culture is grayish white in the beginning, becoming yellow white with age.

When the growth is examined microscopically, it is found to consist of a mycelium of non-septate hyphæ of various thicknesses, with forking divisions and bulbous ends. The hyphæ often show lateral buds and the so-called "yellow bodies" of Kral. The latter may be terminal or lateral upon the hyphæ and contain a condensed cytoplasm that probably escapes when, through internal pressure, the hypha ruptures. It is at such points that the moss-like extensions form. About the fifth day the formation of oïdia occurs, the mycelia dividing into oval elements which remain attached to one another for a long time.

Inoculation experiments made upon human beings were successful in producing the disease. Plant asserts that it is only the cultures containing conidia that are capable of successful inoculation.

Favus usually develops upon the head, the lesions occurring in the hair. It can occur upon other parts of the body, even where no hair is present. Fabry has reported a case of favus of the finger-nails in which the fungus developed between the cells of the corium and epidermis (onychomycosis). Several cases of universal favus are on record.

The lesions of favus vary in size from a pin-head to a dime, are of a sulphur-yellow color, have a saucer shape, and are covered by crusts perforated by hairs. These crusts are known as "favus cups," and consist of a mass of hyphæ and conidia immediately beneath the horny layer of the epidermis in a saucer-shaped depression in the skin. If the crust be separated, a moist, reddened depression remains. The cup itself forms a white, crumbly mass, readily dissolved in water. If the cups are not removed, they unite to form masses, and when the covering epidermis is shed, they appear as dry, yellowish-white, plaster-like masses. The hairs which they contain are lusterless, as if dusty, and are easily withdrawn. The fungi can be observed growing in the shaft as well as in the papilla of the hair. The growth of the fungus in the root sheath may lead to exfoliation of the hair; in the papilla, to atrophy of the root. A more or less marked inflammatory reaction usually occurs in the tissue immediately surrounding the roots of infected hairs.

Mycomycetes.—Mycelium always many-celled. Forming sporangia, conidia, and asci.

Oïdium Albicans.—This organism is the cause of a disease known as *thrush* or *soor*, not infrequently making its appearance upon the tongue, buccal mucous membrane, palate, etc., of marantic infants and adults. The fungus seems to have been first described by Berg, in 1840. It has since been widely studied, though the most important work is that of Roux and Linossier.

The fungus is very pleomorphous, varying according to the specific gravity and chemical composition of the media. The addition of alcohol, sodium lactate, or mannite to the media causes only yeast-like forms to be produced. In cane-sugar preparations single threads, and in gum-arabic and dextrin preparations more extended and more numerous threads, develop. The developmental forms can be more easily and permanently influenced by alterations in the percentage of hydrocarbons in the culture media than by alterations in the nitrogenous constituents. The formation of threads is also favored by diminution of the oxygen, increase of the temperature, the addition of small quantities of nitrates and of toxic substances, or of considerable quantities of acids or alkalis.

The fungus can easily be cultivated upon the usual bacteriologic culture media as well as upon vegetable substances, such as potatoes, beets, melons, etc. It also grows upon milk and in gelatinized beer-wort. The conditions most favorable to development are weak alkalinity, abundant access of air, the addition of sugar and nitrogenous substances to the culture media—peptone, leucin, ammonium tartrate, glycocoll, asparagin, etc. The organism produces a slight amount of fermentation with the evolution of a small amount of alcohol. The colonies are pure white.

The microscopic appearances vary greatly. At times the organism closely resembles the yeasts, and indeed at one time it was classified as a yeast. At other times, however, from the yeast-like elements long cylindric hyphæ, usually consisting of united elongated cells, from which numerous rounded or oval sprouts are given off, especially at the junctions, can be observed. Bulbous swellings are often present upon the ends of the mycelia.

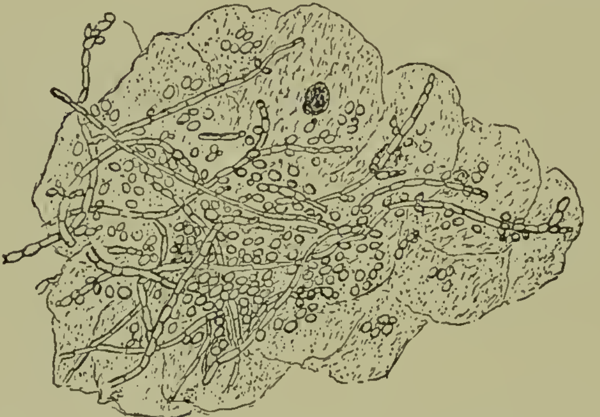

FIG. 122.—A group of vaginal epithelial cells overlaid by mycelial threads and conidia of Oïdium albicans (Smith and Radkey).

In all probability the organism, like its near relative, the *Oïdium lactis*, is a frequent saprophyte, and is able to secure a footing in living tissues only when the vitality of the individual is reduced and the immunity of his mucous membranes partly destroyed. For this reason it is usually met with in cases of infantile marasmus and in adults suffering from such wasting diseases as typhoid fever, tuberculosis, etc. It is most frequently observed in the mouth (see Mycotic Stomatitis), where it forms milk-white patches surrounded by hyperemic zones upon the mucous membranes. The fungus, descending into the epithelium and sometimes into the subjacent connective tissues, causes inflammatory infiltration and superficial necrosis. When removed by divulsion, an abraded surface is left.

Though most frequent in the mouth, the disease has been observed in the esophagus, intestine, vulva, nasal cavities, and middle ear. It has also been observed in an abscess of the liver and in metastatic abscesses of the brain.

Trichophyton Tonsurans.—Closely related to the Oïdium lactis is the Trichophyton tonsurans, the parasite of "barber's itch." It is probably a common saprophyte which, as opportunity presents itself, takes up a parasitic existence upon the skin.

The fungus can be isolated and cultivated, and can be inoculated upon the skin with resulting disease (ringworm). It grows well at the room and incubator temperatures upon the ordinary bacteriologic culture media, forming a white tuft, yellow underneath. The growth consists of mycelia divided into hyphæ and forming abundant conidia.

When parasitic, the organism may grow upon any part of the skin, though by preference upon the hairy parts. It penetrates the shaft of the hairs, causing them to become brittle. When upon the head (*Tinea tonsurans capillitii*), it causes rounded bald areas of various size and scaly, red appearance, from which short hairs stick up here and there. Sometimes small papules, pustules, and crusts appear if the fungi penetrated the hair follicles. When the skin is free from hair, the disease (*Tinea tonsurans vesiculosus* or *squamosus*) appears as red patches with a vesicular or scaly appearance. The patches spread rapidly to new areas, sometimes healing in the first affected areas while spreading to the new ones. The organism multiplies between the horny layer and cellular layers of the epidermis.

Occasionally the parasites grow about the finger-nails, producing *Onychomycosis trichophytina*. The nails are clouded and opaque, become scaly and brittle, and the roots are hyperemic and inflamed.

Microsporon furfur.—This fungus, the cause of *pityriasis, mycosis versicolor, tinea versicolor* or *dermatomycosis furfuracea*, was first observed in 1846 by Eichstedt. It appears in the form of delicate threads with conidia a little smaller than those of the fungi already described. Its cultivation has probably not yet been satisfactorily accomplished, though Spietschka claims to have achieved it.

Upon the skin it causes the formation of pale-brownish or yellowish discolorations, more or less circumscribed, and varying in size from mere dots to extensive areas. The disease occurs on the trunk and limbs, never upon the hands and face.

Microsporon minutissimum.—This organism is the cause of the disease known as *erythrasma*. It is characterized by the small size of its mycelia and conidia. Its successful cultivation was claimed as early as 1851 by de Michelj, who described cultures growing upon potato, agar, and gelatin as forming wine-red or reddish-brown tufts. He also claimed positive results from human inoculations. As seen in culture, the delicate mycelia are either simple or branched, and form chains of short individuals. Bulbous formations frequently seen upon tips of the mycelia are probably incomplete sporangia.

Aspergillus.—Several species of this beautiful fungus are known to be pathogenic, all of them being saprophytic forms whose spores are not uncommon in the air, and accidentally find their way into the body.

The organism is characterized by a loose thallus, consisting of divided mycelia which bear two kinds of fruit upon special hyphæ. The usual fructification is by the formation of conidia. The fruit-bearing hyphæ are elongate and terminate in club-shaped or rounded expansions, from which the sterigma or conidiophores project radially in all directions. The conidia are round and form upon the ends of the sterigma. The result of this arrangement is a fruit which looks not unlike the head of a seeding onion. The conidiophores have various colors, which usually determine the name of the species; thus, Aspergillus niger, A. flavus, etc.

In addition to this asexual sporulation, sexual spores (ascospores) are occasionally formed. A special hypha is observed to terminate in a spirally twisted end which is to become the oögonium. Just behind the spiral several branches grow out and embrace it. One of these, the antheridium or male cell, curves down upon the oögonium, whose cell membrane disappears when the male cell touches it, and the union of the substance of the two cells results from the conjugation. The conjoined cells now become covered by a rounded cellular membrane (the perithecium), and proceed to transform themselves into eight spores (ascospores) which when ripe are liberated by rupture of the perithecium. The ascospores thus formed differ from the conidia spores in that they are not qualified for immediate development, but require an interval of rest; they may, therefore, be looked upon as the permanent spores of the mould.

When the organism grows under unfavorable circumstances, no fruit is produced, though the mycelium develops readily. The typical characteristics of the fungi when artificially set aside are not permanently altered. A. Fränkel frequently transplanted a culture of Aspergillus fumigatus for six months, keeping it all the time at 51° C. During the entire time it produced only sterile mycelia; but when it was again returned to the temperature of 37° C., it at once began to form spores in a perfectly natural manner, and when injected into animals, showed its original virulence.

The aspergilli, in common with the higher fungi, possess the power of storing up reserve stuffs for future use and assuming permanent forms. The form in which this deposition occurs is that of firm, nodular, parenchymatous bodies, which consist exclusively of united mycelial threads surrounded by a dense, dark-colored membrane. Such bodies are called *sclerotia.* The food material is stored up in the mycelial meshwork, and is utilized by the mycelia when they begin to grow afresh under new and favorable conditions.

Aspergillus flavus or flavescens.—The conidia are yellow, yellow-brown, or brown, measure 5 to 7 μ in diameter, and have a warty appearance. The sclerotia are very small and black. The organism grows best at + 28° C.

Aspergillus fumigatus.—This species forms a blue-gray mass much resembling the common penicillium in appearance. The conidiophores are short, terminating in hemispherical ends. Their diameter is about 8 to 20 μ. From the conidiophore spike-like sterigma project in all directions, bearing round, smooth, colorless conidia 2.5 to 3 μ in diameter. Sclerotia are not known. The organism grows best between 37° and 40° C.

Aspergillus niger.—This forms dark-brown mycelial masses. The terminations of the conidiophores are spherical. The sterigma are 2 to 100 μ long, handle-shaped, and branched. The conidia are round, and when ripe, black brown. They measure 3.5 to 5 μ in diameter. The sclerotia are as large as a grape seed and brown red in color. The optimum temperature is 34° to 35° C.

Other described species whose differential characteristics are slight are A. ocraceus, albus, clavatus, oryzeæ, nidulans, subfuscus, etc.

The *pathogeny* of the aspergillus fungi is varied and uncertain. The Aspergillus niger not infrequently excites a suppurative inflammation in the external and middle ear of man. The fungus under these circumstances forms its fruit only near the exterior of the auditory meatus, and within the ear forms mycelia only.

Leber and others have observed Aspergillus fumigatus growing in the cornea and exciting purulent keratitis.

The most interesting and most serious result of the pathogenic action of the fungus is its development in the internal organs of the body, especially the lung, where it leads to what is called aspergillosis, or when the lung is chiefly affected, pneumomycosis aspergillosis. This affection seems to be chiefly caused by the Aspergillus fumigatus, though Aspergillus niger and Aspergillus glaucus have also been found. The disease is most frequent in birds, chickens, ducks, pigeons, parrots, swans, pheasants, flamingoes, etc. It also occurs in mammals (horses and cattle), rarely in man. When the disease does occur in human beings, it is chiefly in those whose lungs are already markedly diseased and whose vital resistance is greatly diminished by tuberculosis or other local disease.

Whether in birds or in mammals, the disease is characterized by purulent focal inflammations in the lungs or other tissues, and a purulent and necrotic pseudomembrane upon the bronchial, tracheal, and other mucous membranes upon which it grows. The appearance of the pulmonary lesions sometimes resembles tubercle, sometimes actinomycosis.

Experimentally, the pneumomycosis aspergillosis is easily produced in birds (pigeons, geese, etc.) by compelling them to inhale aspergillus spores for a few minutes, after which they usually die of pneumonia in a few days.

Olsen and Gade found it easy to kill rabbits by the injection of 100,000,000 or more spores into a vein. Fewer spores failed to produce death, though there were abundant lesions which recovered. The spores always seemed to germinate, though the life of the fungus was probably short and its pathogenesis limited.

The *eurotium* and *penicillium* are interesting though common mould fungi included among the perisporaceæ, but not requiring description here, as they have not thus far been found to cause disease.

Phycomycetes resemble algæ, but are destitute of chlorophyl ; the mycelia are unicellular at first and sometimes become septate. Reproduction is by sexual spores or conidia ; sometimes swarm spores are formed.

Mucor.—The mucors rarely occur parasitically upon animals, in spite of the fact that they are widely distributed in the air and readily grow upon nitrogenous and carbohydrate substrata.

They are characterized by the formation of undivided mycelial threads, forming a dense meshwork. The mycelia are colorless, and the appearance of the mould is at first white, turning gray and often brown as fructification progresses. The fruit-bearing hyphæ are separated from the mycelium at the time of fructification, though they remain firmly attached to the main stalks. They are elongate and usually ascend into the air, though in some species they show interesting curves. They terminate in more or less spherical sporangia, into which they extend as columella. The sporangium is surrounded by a tough membrane which readily softens in water. Within the sporangium a large number of round or oval spores (conidia) are formed, which scatter when the membrane ruptures. The sporangia are sometimes black when ripe, and nearly always have a dark color.

Under certain conditions sexual fructification as well as the formation of asexual conidia may be observed. This is accomplished by the symbiosis of two branches of the mycelia, one of which plays the part of oögonium, the other that of antheridium. The result of the symbiosis is the formation of zygospores.

When the mucors are forced to grow below the surface of a liquid, they frequently assume an oïdium-like appearance and cease to form fruit hyphæ and sporangia.

Many forms of mucors are known—Mucor mucedo, racemosus, stolinifer, macrocarpus, fusiger, aspergillus, phycomyces melitiophtorus, rhizopodiformus, and corymbifer having found places in most books paying particular attention to the subject.

Only Mucor rhizopodiformis and Mucor corymbifer have been described as causes of disease.

Mucor rhizopodiformis.—This species is characterized by a peculiar curve of the fruit hyphæ, which ascend from the thallus toward the free air, then curve down again toward the base. At the point of origin of the conidiophores small processes are given off. These are short and straight, root-like in appearance, and give the name to the fungus. The sporangia are dome-like at the distal surface and contracted near their attachments. The spores are colorless. Cultures of this species give off a pleasant, fruit-like odor.

Mucor corymbifer.—In this species the mycelia are gray white. The conidiophores do not ascend perpendicularly, but are widely extended and hang down. The hyphæ bearing the sporangia branch. The sporangia are top-shaped and colorless. The spores are also colorless, very small, and somewhat elliptic in shape.

The mucors occasionally make their appearance in the external ear of man and occasion inflammation. Paltauf has observed a case of generalized mucor infection in man. The man was a day-laborer who died with enteritis, circumscribed peritonitis, ulcers of the intestines, focal areas of pneumonia in the lungs, abscesses of the brain, and phlegmonous inflammation of the pharynx and larynx. In all the lesions Paltauf was able to demonstrate the presence of the mycelia, and in the lung the fructification of a mucor which he supposed to be Mucor corymbifer.

The injection of the spores of the mucors into the ear vein or into the peritoneal cavity of rabbits causes death, with distribution of the fungi throughout the body and the appearance of their mycelia in the kidneys, lungs, liver, etc. Dogs are immune against the mucors.

Blastomycetes.—The saccharomycetes or yeasts have up to the present time attracted little attention as etiologic factors of disease, though to the chemist and brewer they are of the greatest importance, and many species have been cultivated and studied. The best known are *Saccharomyces cerevisiæ et vini.*

The blastomycetes are microscopic, spherical or ovoid, chlorophylless, unicellular, vegetable organisms, whose chief peculiarity is reproduction by budding. From one or both ends, or sometimes from sides of the cells, small buds make their appearance, gradually increasing until a considerable size is attained, when the daughter cell is detached and takes up an independent existence. In some cases the daughter cells remain adherent to the parent cells, even after they have themselves begun to bud. The structure of a yeast plant is exceedingly simple, and consists of a protoplasmic body surrounded by a double-contoured capsule. Sometimes the cytoplasm contains drops of fat, granules, and vacuoles. The existence of a definite nucleus is doubtful. Under certain conditions the yeast cells sometimes develop into long cylindric hyphæ, suggesting the mycelial threads of the moulds. These most frequently occur in old cultures upon the surface of liquids and in contact with the air. This hypha formation suggests close relationship with the oïdia on the one hand, and through the genus *Phragmidiothrix* with the bacteria and yeasts on the other hand.

Hansen has also shown that the yeasts not only multiply by gemmation, but also by sporulation (formation of ascospores) and that it is probably by means of these that the species secures permanence. He found that the spores are produced only by young and vigorous cells; that they are produced only upon moist surfaces plentifully supplied with air, and that the temperature most favorable for this formation is 25° C. By a careful study of the germination of the spores, Hansen was able to divide the saccharomycetes into three groups:

In the *first*, to which S. cerevisiæ belongs, the first stages of germination are attended by so marked a degree of expansile force upon one another while still inclosed in the mother cell as to lead to the formation of what are described as partition walls in the cell. This partition wall at first consists of the spore walls with the mother plasm squeezed between them. During further development, however, a complete union of the walls takes place, so that a true partition wall results; the cell then becomes a compound spore divided into several chambers. During germination the spores swell and the wall of the mother cell, which originally was moderately thick and elastic, stretches and consequently grows thinner. It is finally ruptured, and then remains as a loose or shriveled skin partially covering the spores, or it may gradually dissolve during germination. Budding can occur at any point on the surface of the swollen spores. After buds have formed the spores may remain connected or they may soon be detached from each other.

The *second* type occurs in the case of S. Ludwigii, when fusion takes place in the very first stages of germination; in each case, however, it is the new formations and not the spores which grow together. These new formations are further distinguished from the previous type in that they are not yeast cells, but mycelium-like growths (promycelium). The development of yeast cells takes place from this promycelium, a sharp partition wall being first formed; the cell is then detached and its ends finally rounded. At the ends of these cells buds are developed, and these also split off at the partition walls. In the case of the older spores this curious fusion is more uncommon. Some germ filaments develop into a branched mycelium.

The *third* type, which occurs in S. anomalus, is distinguished from the former in that the spores are of quite a different shape. They are also semi-spherical, with a rim at the base. During germination the spore swells and the projecting rim may either remain or disappear. Buds then make their appearance at different points on the surface of the spore.

In addition to the ascospores, Will has observed what he describes as "durative cells." They are round or oval cells with thick membranes, and contain a number of small oil drops. When they germinate, globular or elongate yeast cells, singly or in large numbers, are formed. Sometimes peculiar club-shaped cells are formed from them. They are regarded as "durative cells," because they are most numerous in old cultures, and have been found alive after all the other cells have died.

The common forms of yeast seem to be devoid of pathogenic powers, and when injected into animals, produce no results. Raum found that the intravenous injection of some species caused dyspnea, fever, subnormal temperature, collapse, and death. No lesions were observed except the obstruction of the pulmonary blood vessels by the accumulated yeast cells.

Rabinowitsch also succeeded in showing that in large doses various yeasts were pathogenic for small laboratory animals.

Many writers at the present time seem convinced that the Russell fuchsin bodies in carcinoma, the bodies of Sanfelice, Mafucci and Sirleo, Ruffer and Walker, Walker and Plimmer, and Plimmer, all belong to the blastomycetes, and speak of them as pathogenic yeasts. It cannot be said that there is any considerable evidence in favor of this view, and it is extremely doubtful whether the bodies seen in carcinoma cells are blastomycetes, and still more questionable whether the cultures supposed to have been made from the tumors are identical with the microscopically demonstrable bodies. It is not impossible that yeasts might be accidentally present in carcinomata, just as bacteria commonly are, but that they are the cause is by no means demonstrated. None of the inoculations made with the well-known varieties of yeasts has been productive of any tumor-like developments, and those resulting from the inoculation of Plimmer's cultures did not resemble the tumors from which they were obtained.

Busse claims to have discovered a pathogenic yeast in the giant cells of osteosarcoma, to have cultivated it and successfully inoculated it into animals. It always maintained its yeast form. Its inoculation into animals, however, was followed by suppuration, not by sarcoma.

One of the most interesting as well as truly pathogenic effects which may follow blastomycetic infection is found in the cases of *blastomycetic dermatitis* described by Gilchrist. The fungi present appeared as good-sized oval, disk-like bodies, highly suggestive of yeasts and failing to take any of the ordinary stains.

Schizomycetes or Bacteria.—The bacteria are unicellular vegetable organisms of simple structure and of exceedingly minute dimensions. They are all microscopic, and many of them are so small that the highest powers of the microscope give us only the most inadequate idea of them. The bacteria are the smallest known living things. Indeed, we are daily becoming more and more convinced that, beyond the defining power of our microscopes, there are organisms too small to see, known to us only by their effects.

Bacteria are in all probability the most important enemies with which the higher animals have to cope. Their distribution is so universal, their capacity for enduring unfavorable conditions so pronounced, their multiplication subject to so few limitations, and their products so frequently detrimental, that there is scarcely an individual among the higher organisms, and particularly among the warm-blooded animals, that does not, during some part of his life, become their victim. Indeed, it might be well said that that individual is fortunate who escapes death from them.

There are probably no forms of life so widely distributed in nature as the bacteria. The soil has an extensive flora, waters of nearly all kinds contain numbers of them, the bodies of animals are habitually infected by them, and from these bodies they are continually being discharged upon fresh soil and into new waters. Indeed, many of the familiar operations that go on about us, and upon which we have long ceased to look with surprise, are the work of bacteria. Thus, the putrefaction and dissolution of animal matter depend essentially upon bacteria. Many of the fermentative processes that go on in carbohydrates are the work of bacteria. The formation of cheese is in part the work of bacteria. The ripening of cream preparatory to making butter is accomplished partly by bacteria. Many of the familiar diseases depend upon bacteria, and we find these microscopic entities on every hand, sometimes performing benign offices for us, sometimes afflicting us with most malignant disease.

The importance of bacteria in medicine, hygiene, chemistry, and the arts has stimulated careful research concerning them in all these departments, and has brought together the information and technic of investigation which we speak of as *bacteriology*. At one time all that was known of the subject could be told in a chapter of a text-book, but at present the student must be referred to text-books upon bacteriology for any adequate knowledge of it. The bacteria were thought by Leeuwenhoek, Ehrenberg, Dujardin, and others to be animalculæ belonging to the infusoria, and were consequently placed by them in the animal kingdom. All their characteristics indicate that they are vegetable forms, however, and now that our present knowledge of them has advanced so widely, we unhesitatingly place them among the lowest orders of the thallophytæ. Their exact position is, however, purely speculative, and our classifying them among the fungi is to be looked upon as provisional, as it is characteristic of the fungi that they contain no chlorophyl, which the bacteria frequently do. Whether, therefore, it is more correct to place them among the fungi or among the algæ, or to make for them a separate group, is doubtful, and probably cannot be determined until our knowledge of their biology undergoes further progress. It is customary to differentiate the bacteria from the moulds and yeasts by using the term *schizomycetes* as referring to the whole group.

The classification of the bacteria themselves is almost as difficult with the knowledge we now possess of their biology as properly to place them in the general system. Various attempts have been made, nearly all the morphologic peculiarities being seized upon as differential features. Probably the best and most scientific system is that of Migula, a slight modification of which is as follows:

I. **Family Coccaceæ.**—Cells globular, becoming slightly elongate before division, which takes place in one, two, or three directions of space. Formation of endospores very rare.

1. *Streptococcus.*—Division in one direction of space only, producing chains of organisms like strings of beads. No flagella.

2. *Micrococcus.*—Division in two directions of space, so that fours or tetrads are often formed. No flagella.

3. *Sarcina.*—Division in all three directions of space. Leading to the formation of bale-like packages of cocci. No flagella.

4. *Planococcus.*—Division in two directions of space, like micrococcus. Flagellated.

5. *Planosarcina.*—Division in three directions of space, and like sarcina, but provided with flagella.

II. **Family Bacteriaceæ.**—Cells more or less elongate, cylindric, and straight. Never form spiral windings. Division in one direction of space only, transverse to the long axis.

1. *Bacterium.*—Without flagella. Occasional endospores.

2. *Bacillus.*—Flagella arising from all parts of the surface. Endosporulation usual.

3. *Pseudomonas.*—Flagella attached only at the ends of the cells. Endosporulation rare.

III. **Family Spirillaceæ.**—Cells spirally twisted like a corkscrew, or short and curved and representing segments of the spiral. Division transverse to the long diameter.

1. *Spirosoma.*—Rigid. Without flagella.

2. *Microspira.*—Rigid. One, two, or three undulating flagella attached to the ends.

3. *Spirillum.*—Rigid. From five to twenty semi-circular or undulating flagella attached to the ends.

4. *Spirochæta.*—Serpentine and flexile. Flagella not observed. Movement probably accomplished by means of an undulating membrane.

IV. **Family Mycobacteriaceæ.**—Cells forming more or less elongate, cylindric filaments, often clavate-cuneate or irregular in form. No endospores, but formation of gonidia-like bodies due to segmentation of the cells. No flagella. Division transverse to the long diameter. Not surrounded by a sheath as in chamydobacteriaceæ.

1. *Mycobacterium.*—Cells in their usual form, short cylindric rods, often bent and irregularly cuneate. At times Y-shaped forms or longer filaments with true branchings. Sometimes produce short coccoid elements, perhaps gonidia. (This genus includes the corynebacterium of Lehmann-Neumann.)

2. *Actinomyces.*—Cells in their ordinary form occur as long branched filaments. Produce gonidia-like bodies. Cultures usually have a mouldy appearance, due to the development of aërial hyphæ.

V. **Family Chamydobacteriaceæ.**—Vary in different stages of their development. Characterized by a surrounding sheath about both branched and unbranched threads. Division transverse to the length of the filaments.

1. *Cladothrix.*—Characterized by *pseudo*-dichotomous branchings. Division only transverse. Multiplication by the liberation of whole branches. Transplantation by means of flagellated swarm spores which are actively motile.

2. *Crenothrix.*—Cells united in unbranched threads, which in the beginning divide transversely only. Later the cells divide in all three directions of space. The products of final division become spherical and serve as reproductive elements.

3. *Phragmidiothrix.*—Cells at first united into unbranched threads. Division in all three directions of space. Late in development, by the growth of certain cells through the delicate, closely approximated sheath, branched forms are produced.

4. *Thiothrix.*—Unbranched cells inclosed in a delicate sheath. Non-motile. Division in one direction of space. Cells contain sulphur grains.

VI. **Family Beggiatoaceæ.**—Cells united to form threads, which are not surrounded by an inclosing sheath. The septa are scarcely visible. Division transversely only. Motility accomplished through an undulating membrane.

Beggiatoa.—Cells contain sulphur grains.

While on all sides admitted to be the best biologic and scientific classification of the bacteria yet achieved, Migula's nomenclature has not met with universal acceptance, and doubtless it will take a long time before the old names and terms, for which we have a kind of sentimental fondness, can be replaced by the more correct ones.

At the present time, therefore, we speak of any small spherical bacterium as a *coccus* or *micrococcus*. If it divide in one direction and the individuals cling together in pairs, it is called *diplococcus;* if in rosary-like chains, *streptococcus*. If the division is in two directions of space and the individuals remain attached, the little groups are frequently called *tetracocci;* the larger groups, *merismopedia*. Division in three directions gives us cubical aggregations which can aptly be compared to bales of goods tightly bound; this is known as *sarcina*. It commonly happens that the division of the cocci occurs without definite relationship or arrangement of the resulting cocci, which form irregular clusters as well as strings and pairs. This variety is commonly spoken of as *staphylococcus*.

The majority of the cocci are very small. Few are motile, very few being flagellated. Sometimes individual cocci, sometimes definite clusters of them, swim rapidly. Occasionally chains of streptococci swim with an undulating movement. The formation of endospores is rare among the cocci, though arthrospores are said to be common. "Cohn was the first to observe that sometimes single cells that become detached from a filamentous bacterium, or that are set free by the breaking-up of the filament, do not possess the character of ordinary vegetative cells, but rather resemble the gonidia, conidia, or spores, such as are found in some algæ or moulds, and Hueppe and De Bary subsequently showed that in many bacterial species single members of a chain may acquire the resisting properties and the function of the resting stage. For distinction these were called *arthrospores*." . . . "It appeared in some instances as if almost any individual cell, while not unlike the others in form, might, under certain conditions, become an arthrospore." . . . "Hueppe observed that such a cell would sometimes be insulated or protected against harmful influences by a mantle of the adjacent dead cells formed about it. In some cases the arthrospores increase in size and acquire a compact membrane, as happens in some algæ." . . . "True arthrospores are spherical in form, but this fact must not lead us to confound them with the polar granules produced by plasmolysis."

In common parlance, any micro-organism with one diameter distinctly greater than the other, and not curved or twisted, is called a *bacillus*, the terms *bacterium* and *pseudomonas* being much less frequently employed. The bacillary forms of all three genera, but chiefly of the genus *bacillus*, form *endospores*. "Endospores were discussed by Perty in 1852. It is necessary to distinguish two kinds of endospore formation, which, however, are connected with one another through intermediate forms. In bacteria of the first and more comprehensive type a dark speck appears in the cell contents after—but sometimes without—preliminary granulation. This speck becomes gradually larger, and reaches its ultimate size at the expense of the cell protoplasm. In a colony of bacteria different stages of spore formation may be simultaneously observed. By contraction of the protoplasm and decrease in the quantity of water contained the spore comes to have a highly refractive appearance. Its body becomes limited externally by a dense and rapidly forming spore membrane. The motile forms become motionless before spore formation. It is a matter of secondary significance that sometimes all the cell protoplasm is converted into a spore, and that sometimes a portion remains outside. It is likewise of subordinate importance whether the spore be round, oval, or bean-shaped; whether it is formed at the middle of the cell or at the end; whether the cell preserves its form or suffers a preliminary swelling at the place where the spore is to form." . . . "In the germination of spores, likewise, similar small and inconsiderable differences make their appearance. These characters are in certain cases very important as aids to diagnosis, but are not so essential as the difference shown by the second type of endospore discovered by Peters and L. Kline. In this there is an initial separation of the protoplasm into a spore-forming and a spore-free portion, so that from the beginning the spores are sketched out in their final size and shape and do not, as in the first type, gradually increase their substance at the expense of the rest of the protoplasm. During the process of maturation the nutrition of the spore rudiment is provided for by the rest of the cell protoplasm, and, as the cilia bear witness, the movements of these species do not cease during spore formation."

The germination of the spores is not without interest, especially in the ovoid and bean-shaped forms. The germinating spore changes its clear cytoplasm by the development of fine granules, and its circumscribing capsule seems to attenuate. There is gradual increase in size, and finally the capsule bursts open and the young bacillus escapes. The opening for the escape of the spore takes place at the middle in some species, at the pole in others. This equatorial or polar escape is so constant for different species that Migula has made use of it for purposes of differentiating them.

The spore production is limited to one spore for each bacillus. It may develop at the center of the cell, toward one end, or at one end of the cell. When the spore is situated at one end and is greater than the bacillus in diameter, a drumstick form is produced, which the Germans describe as a "Trommelschlager." When centrally situated and occasioning distention of the organism by its large size, it is called a *clostridium*. When the formation of the spore is complete, the disintegration of the parent organism begins.

Many of the bacillus and pseudomonas forms are actively motile because of their *flagella*. These organs of locomotion are more or less elongate, undulating or curled, extremely delicate filamentous projections of the cytoplasm through the cell-wall. They are too fine and too delicate to be detected by ordinary examination, though readily observed in properly stained specimens. There may be a single flagellum attached to one end of the organism (monotricha), or there may be a flagellum at each end (amphitricha), or there may be a number of them attached to one or both ends (lophotricha), or the flagella may be numerous and distributed over the entire body surface (peritricha).

Some of the cocci and a few of the bacilli are said to be encapsulated—*i. e.*, they are surrounded by what seems to be a thick gelatinous or mucous investiture, which may depend upon swelling or softening of the cell-wall, or upon some secretion which the organism collects about it as a mantle. The office of this capsule is not known. It is well seen in stained specimens of the pneumococcus in sputum or blood, and in stained specimens of the Bacillus aërogenes capsulatus, Pfeiffer's capsule bacillus, and others.

The occurrence of branched bacilli is often mentioned, and has given rise to considerable speculation as to what the projections and branches may mean. It is now pretty generally accepted that they indicate greater complexity of structure than belongs to the bacilli, and that the species in which they occur should properly be classed among *mycobacteriaceæ* or other higher bacteria.

An elongate organism of corkscrew shape or forming a distinct arc of a circle, suggesting the possibility of developing a corkscrew shape, is called a *spirillum* if rigid, a *spirochæta*, if flexible. Migula calls similar forms without flagella *spirosoma*. By French writers they are nearly always referred to as *vibrio*, though these writers also apply the term *vibrio* rather carelessly to bacillary forms, especially if they undulate in swimming. Spiral organisms with pointed ends are sometimes called *spirulina*: those of flattened form, bearing a resemblance to a twisted ribbon, *spiromonas*. A spiral organism spotted with contained sulphur granules has been described as *ophidiomonas*.

The spiral organisms are nearly all motile, and with the exception of the genus *spirosoma* are flagellated. The formation of endospores is common. The organisms may be so short as to resemble commas, or may be very long and present many corkscrew-like twists.

Of the *mycobacteriaceæ*, the best known is that familiar to us under the name *actinomyces*. It may perhaps be accepted as a type of the genus.

The actinomyces may be said to occupy a kind of midway position between bacteria and moulds. Their vegetation resembles the moulds in that it consists of a branched network of delicate filaments, upon which a downy development of aërial hyphæ takes place. Upon careful examination, however, it is found that the filaments are extremely delicate, like bacillary threads, and not distinctly and doubly contoured like the mycelia of the moulds.

The delicate rod-like filaments divide dichotomously. Some of the filaments are long and straight, some straight and branched, some closely twisted like the spirilla, some divided into short, rounded individuals resembling cocci, and are possibly reproductive elements, while others are expanded into club-shaped enlargements, which are probably involution forms. The delicate threads, the lack of distinct encasing membranes and of reproductive cells and conidia, clearly separate the organisms from the moulds. Just what the different elements signify is not clear. Some of the coccoid elements are probably spores, though they differ in certain particulars: as, for example, in their resistance to the penetrating action of the dyes and to heat. The mycelia are destroyed by a brief exposure to 60° C., but the spore forms resist 75° C. for five minutes.

The actinomyces grows, like other bacteria, in all the usual media—agar, blood serum, gelatin, bouillon, etc. When one of the colonies is touched with the platinum wire, the aërial filaments with their spores are disturbed and the spores alone removed. If, however, one teases one of the dense colonies, branched threads become visible. The vegetation upon artificial media corresponds almost perfectly with the organism as it occurs in the tissues. The central part of each consists of a branched, thready mass, in which, together with the straight filaments, coccoid and spirilloid forms are present. The coccoid forms are often gathered together like strings of beads. Extending from the central mass so as to project radially in all directions—very rare in the artificial cultivations, but nearly always present upon the organism as it occurs in the lesions—are the radiating, club-shaped elements which give the organisms the name "ray fungus." The significance of these clubs is not known. At one time they were supposed to be organs of fructification, but at the present time they are thought to be swollen and degenerated filaments which are injured by contact with the surrounding tissue.

In well-stained specimens, however, the filament to which it is attached can be seen to enter the proximal end of the club. The clubs may be regular in outline and fusiform or club-shaped, or they may partially divide into finger-like segments at the distal end. They are of low vitality and readily disintegrate. The youngest colonies obtained from actinomycotic pus have no rays or clubs, but form grayish, gelatinous, homogeneous, compressible bodies of almost mucus-like consistence. These consist exclusively of thread-like elements.

Biology of the Fungi.—*Relation to Oxygen.*—Like all living things, the fungi require oxygen, though certain forms of bacteria are peculiar in their relation to it. In consequence, it is customary to divide the organisms into *aërobic* forms, which can, and *anaërobic* forms, which cannot, live in the presence of uncombined oxygen. The anaërobic forms obtain oxygen by the analysis of compounds containing it. Many bacteria are indifferent in their behavior to oxygen. Their ability to grow in nature seems to depend upon association with other organisms, by which the free oxygen is absorbed. B. tuberculosis and B. diphtheriæ seem to be almost purely aërobic; B. tetani and B. œdematis maligni, purely anaërobic. When a micro-organism is able to maintain its existence equally well with and without free oxygen, it is called an *optional anaërobe;* when able to grow only in combined oxygen, an *obligatory anaërobe.*

The human body affords opportunities for the growth of both aërobic and anaërobic organisms, containing both well-oxidized and meagerly oxidized tissues. The ability of the anaërobic forms to grow parasitically may be facilitated by other organisms accidentally introduced with them. This, however, does not explain all cases, for animals die readily of tetanus after inoculation of pure cultures into the subcutaneous tissues, the bacillus being able to endure the absorbed oxygen in the tissue juices.

Relation to Food.—The moulds and yeasts and many of the bacteria can grow quite well upon carbohydrates, but most of the bacteria do better upon a substratum containing proteids. The simplicity of the compounds upon which they can live is shown by the composition of the following fluids:

PASTEUR'S MEDIUM.

Distilled water	100 parts.
Cane-sugar	10 "
Ammonium tartrate	1 part.
Ashes of 1 gm. of yeast.	

USCHNISKY'S MEDIUM.

Water	1000 c.c.
Glycerin	3 to 4 gm.
Sodium chlorid	5 to 7 "
Calcium chlorid	1 "
Magnesium sulphate	2 to 4 "
Bipotassium phosphate	2 to 2½ "
Ammonium lactate	6 to 7 "
Sodium aspartate	3 to 4 "

PROSKAUER AND BECK'S MEDIUM.

Ammonium carbonate	0.35 per cent.
Potassium phosphate	0.15 " "
Magnesium sulphate	0.25 " "
Glycerin	1.00 " "

In artificial culture in the laboratory the moulds and yeasts grow luxuriantly upon moist bread-crumbs and potato, the bacteria upon beef-broths or beef-broths solidified by the addition of gelatin or agar. Such media should contain about 80 per cent. of water and 0.5 per cent. of sodium chlorid. Very few micro-organisms can grow upon dry nutrient material, water being essential to active life. The *reaction* of the substratum is of great importance to many forms. The moulds do best upon media with a slightly acid reaction; the bacteria upon media with a feebly alkaline reaction.

The fungi are unable to live upon purely inorganic matter. The purely saprophytic forms are able to grow luxuriantly upon almost any culture medium, while of the purely parasitic forms, some, such as the lepra bacillus, have very rarely been successfully cultivated. Of the important pathogenic forms, each has its particular appropriate medium upon which artificial culture is best achieved—glycerin-agar for the tubercle bacillus, blood serum for the diphtheria bacillus, hemoglobinized agar for the influenza bacillus, mixtures of agar and blood serum for the gonococcus, etc. In the consideration of individual species, these peculiarities of appetite should not be forgotten.

Relation to Temperature.—The temperatures at which bacteria live have a wide range. A few organisms known as *thermophilic* bacteria live in hot springs and pools and thrive at 60° to 70° C., temperatures at which all other micro-organisms cease to grow, and at which the greater number of them are killed. The pathogenic parasitic forms thrive best at temperatures approximating those of the animal body in health and disease. Saprophytic organisms grow at much lower temperatures. Flügge found that Bacillus subtilis grew very slowly at 6° C., and until 12.5° C. was reached fission did not occur oftener than every four or five hours. At 25° C. fission occurred every forty-five minutes, and at 30° C., every thirty minutes. When the temperature reaches 40° C. the growth is less rapid, and beyond 42° C. it again becomes slow and soon ceases. The bacilli are killed between 60° to 65° C., though their spores are able to endure 100° C. for some time. All known fungi and their most resisting spore forms are destroyed by dry heat at 150° C. maintained for a short time, and by steam under pressure, so as to bring the temperature to 120° C. in a few minutes. Most spores are killed by exposure to streaming steam of 100° C. for more than five minutes, though a few can be steamed for an hour without harm. Nearly all asporogenous bacteria are killed by temperatures beyond 75° C. maintained for thirty minutes.

Cold is injurious to bacteria, and freezing and exposure to extreme degrees of cold, such as can be secured by liquid air, kill great numbers of them. A few individuals of each species, however, always survive even these extremely low temperatures so that cold is less destructive to bacteria than heat.

Relation to Light.—Micro-organisms vary in the effects resulting from exposure to light. The saprophytic organisms live for the most part in daylight, and often in direct sunlight, without injury. In the laboratory, however, it is found that many bacteria, and especially the parasitic forms, are injured by exposure to concentrated light. When cultures of some of the pathogenic forms are exposed to sunlight, they fail to grow upon transplantation, and are presumably killed. When kept growing exposed to diffused light, some of the pathogenic forms attenuate more rapidly than when kept in the dark. Some of the moulds grow slowly in the light and rapidly in the dark. Bacillus mycoides roseus is said to produce its pigment only in the dark.

Blue is distinctly prejudicial in its influence upon bacteria, and when Petri-dish cultures are thickly sown with colonies, and an area of the dish covered by a blue glass or paper, the growth of the colonies within the confines of the colored area is so restrained that, upon removing the color, its outline is evinced by the small size and diminished number of colonies.

Relative to Physical Conditions.—*Electricity.*—The studies made to determine the effects of continuous and interrupted electric currents upon bacteria are few in number and conflicting in result. Very powerful currents are said to kill the organisms, change the reaction of the culture media, and alter whatever toxins may be present in the culture.

X-rays.—The micro-organisms are apparently unaffected by the *x*-rays, though it is said that prolonged exposure to their action lessens the vitality and diminishes the virulence of the organisms.

Movement.—The condition of rest seems best adapted to micro-organismal life. Rapid movement seems to inhibit growth. This may explain why bacteria usually do not grow in large numbers in the rapidly circulating blood, and also explains why rapidly flowing streams, frequently interrupted by rapids and waterfalls, furnish better drinking-water than sluggish streams.

Relation to Chemical Agents.—Reaction is of great importance to micro-organisms. The moulds seem to prefer substrata with acid reaction; the bacteria with alkaline reaction. Some organisms grow equally well upon acid and alkaline media; others cannot be grown artificially unless just the right degree of acidity or alkalinity is prepared for them. The physiologic activities of bacteria may vary according to the reaction; thus, when Bacillus prodigiosus grows upon slightly acid media, it is colorless; but when it grows upon alkaline media, it produces a beautiful red color. Bacillus diphtheriæ grows in slightly acid media, but produces toxin only in alkaline media.

These variations in metabolism caused by slight variations in reaction should not be neglected in reflecting upon the pathologic processes in which bacteria are concerned.

Strong acids or alkalies inhibit micro-organismal growth, and very strong acids or alkalies destroy them.

Salts.—Various salts exert a marked influence upon bacteria, though how they act is unknown. In all probability sodium chlorid and some of the common widely distributed salts are of importance to the organisms in aiding diffusion processes. Excessive quantities of various salts may tend to bring about bacteriolysis.

The salts capable of forming compounds with albuminous substances usually behave deleteriously upon micro-organisms, combining with their protoplasm and thus destroying them. Of these, the mercurial salts, especially the biniodid and bichlorid, are the best known. The caustic substances, such as nitrate of silver, caustic potash, and caustic soda, are destructive, sometimes even in great dilution.

Chemical substances that inhibit the growth of bacteria are known as *antiseptics;* those that kill them, as *germicides.*

Alcohols and ethers behave differently toward micro-organisms. Ethyl alcohol in weak solutions does not affect micro-organisms, but stronger solutions destroy them in time by dehydration. Alcohol does not injure spores.

The ethers are devoid of energetic action upon micro-organisms.

Carbolic acid is peculiar among the alcohols for its extremely energetic action, being one of the best disinfectants and germicides known. Its power in this direction, however, is distinctly limited, and its employment for disinfecting purposes is usually in 5 per cent. solution. This solution kills the majority of micro-organisms in a few minutes, though the resisting spores of anthrax and some other bacteria may enable them to endure such solutions for twenty-four hours.

Formaldehyd is one of the most powerful and useful disinfectants known. The gas itself is a strong disinfectant, and can be used for disinfecting rooms, hospitals, and ships, while in solutions it is probably more useful and more powerful. It is destructive to nearly all bacteria in solution of 1 : 20,000 to 1 : 5000.

Gases.—The necessity of oxygen in micro-organismal life has already been discussed. Nitrogen and hydrogen are indifferent to them, and anaërobic bacteria grow well in atmospheres of either. Carbon dioxid and sulphureted hydrogen are poisonous to micro-organisms. In general, it may be said that gases poisonous to animal life are also poisonous to vegetable life, and in consequence chlorin, bromin, iodin, sulphurous oxid, and others are very destructive and may successfully be employed for disinfecting purposes.

Relation to Moisture.—Micro-organisms are with few exceptions designed to live upon moist substrata. Bacillus prodigiosus has been found growing upon dry crackers, but even it thrives best when in the presence of abundant moisture. For this reason it is recommended that artificial cultures of bacteria be grown upon media containing about 80 per cent. or more of water.

The effect of desiccation upon bacteria is deleterious, and whenever bacteria are dried, large numbers of them probably die. Enough survive in most cases, however, to maintain the species. It is said that the spirillum of Asiatic cholera can withstand drying for nine months, and that Bacillus typhosus and Bacillus prodigiosus can remain alive for a year and a half. Other bacteria die quickly when dried; thus, the streptococcus may not live longer than a week. In experiments made to determine the duration of life in the dry state, one should not lose sight of the fact that other factors come into prominence. Dried organisms, for example, are exposed to an unusually active oxidation, etc.

The spores of micro-organisms seem to be particularly adapted to live in the dry state, and those of anthrax, if dried upon silk threads or in filter-paper, can be kept alive for years.

Association with other Micro-organisms.—It is interesting to observe that the fungi act upon one another in many ways. The large class of lichens are now known to be fungi growing parasitically upon algæ. The growth of the tetanus bacillus in the soil is supposed to depend upon associated bacteria by which the oxygen is used up. As bacteria grow together they not infrequently destroy one another; thus, in cultures from the throats of diphtheria suspects, it not infrequently happens that the Bacillus pyocyaneus is present and destroys the diphtheria bacilli in time. As the culture is incubated, the diphtheria bacillus at first grows, forming a yellowish-white layer upon the medium. Later on the Bacillus pyocyaneus begins a vigorous growth, overgrows the diphtheria bacilli, and brings about their ultimate solution, possibly through a bacteriolytic enzyme (*pyocyanase* of Emmerich and Low (?)). Should an acid-producing organism grow hand in hand with the diphtheria bacillus, the latter would not generate toxin as usual. Contaminating organisms in tetanus cultures sometimes entirely destroy the toxin, so that, although many tetanus organisms are present, the filtered culture is inert or feeble in toxic action.

Bacteria attenuated by prolonged cultivation in the laboratory or by drying can often be greatly increased in virulence by inoculation into susceptible animals together with some harmless organism, such as Bacillus prodigiosus, by which the conditions under which it grows in the body are altered. On the other hand, sometimes the operation of a pathogenic bacterium is checked or altered by the accidental presence of some harmless organism.

The reader must not lose sight of the very important truth that in our experimental work we habitually investigate the effects of *pure cultures* upon animals, though nearly all spontaneous infections are mixed, for one or another reason some particular micro-organism predominating over others and determining what the course of events shall be.

Chemistry of Micro-organismal Life.—*Putrefaction and Fermentation.*—It is impossible for micro-organisms to live upon and appropriate to their own uses elements obtained by the cleavage of complex molecules without chemical alteration of the substratum. By these means the familiar phenomena of putrefaction and fermentation occur. It is by processes analogous to these that fungi elaborate those peculiar alkaloidal substances which are known as *ptomains*.

Ptomains.—" A ptomain is a chemical compound, basic in nature, formed by the action of bacteria (and other fungi) upon organic matter." It is the result of the process which we describe as *putrefaction*, and can be correctly called a *putrefactive alkaloid*. Some ptomains are poisonous; some not. They play very little part in pathology. They may be inadvertently consumed with food and occasion poisonings, such as are familiar from spoiled ice-cream and meat. Sapremia, from gangrenous members of the body, depends upon products of putrefaction absorbed into the body by the lymphatics.

It may, therefore, be said with very little reserve that ptomains have little to do with pathologic processes, because their origin depends upon putrefactive changes which must, as a rule, be of long duration before discoverable quantities are formed, and because most of the ptomains formed in the body are harmless in the quantities in which they are produced. The bacteria of fermentation are called *zymogenic;* those of putrefaction, *saprogenic.*

Gases.—The disruption of complex molecules is also a source by which gases are liberated from substrata upon which bacteria grow. According to the composition of the substratum and the variety of micro-organisms will the gases vary in nature. Those most commonly encountered in measurable quantity are hydrogen and carbon dioxid. Ammonia, sulphureted hydrogen, marsh-gas, and others may be formed. Gaseous edema sometimes results from certain forms of infection. Gas-producing bacteria are called *aërogenic.*

Odors.—The evolution of ammonia and sulphureted hydrogen is naturally attended with odor, but in addition aromatic substances are produced by the putrefactive processes as well as by the metabolic excretions of the bacteria, and cultures of different organisms have in many cases characteristic odors. Every one who has cultivated Bacillus tetani is familiar with its peculiar odor, and the pungent odor of Bacillus mesentericus vulgatus is familiar to every student of bacteriology.

Of the aromatic substances produced by bacteria, *indol* is the most common, and is made use of for the differentiation of species, as Spirillum choleræ asiatica and Bacillus coli communis. Phenol, kresol, hydrochinon, hydroparacumaric acid, and paraoxyphenylacetic acid are by no means uncommon products of putrefaction.

Pigments.—Bacteria, yeasts, and moulds may produce pigments. They are usually formed outside of the bodies of the organisms, in the molecular matter between them; but sometimes the pigment granules are in the cells. The chemistry of these pigments is obscure. Some, as pyocyanin, are ptomains.

The pigments are for the most part insoluble in water, and, therefore, do not saturate the culture media (agar) upon which the organisms are grown. Occasionally, as in the case of fluorescin and pyocyanin, the pigments are soluble and readily penetrate the agar.

The blue pigment of Bacillus janthinus, the brick-red of Bacillus prodigiosus, the beautiful orange of Sarcina aurantiaca, the coal-black of the Saccharomyces niger, etc., form striking characteristics by which the species can often be recognized. The pigments are for the most part produced by saprophytic organisms.

Organisms producing pigments are called *chromogenic;* those producing none, *non-chromogenic.*

Phosphorescence.—Bacteria, for the most part isolated from sea-water, sometimes occasion a peculiar phosphorescence in cultures made with sea-water as the basis. The phenomenon is marked, and the light emitted from several tubes of highly phosphorescent bacteria may enable one to see the face of a watch in the dark.

Phosphorescing bacteria are called *photogenic.*

Acids and Alkalies.—In fermentation and putrefaction the chemical changes are associated with marked changes in reaction. One of the most familiar examples of this is seen in the change of acid to strongly alkaline urine, as saprophytic bacteria transform the urea to ammonium carbonate. In all putrefactive processes associated with the formation of ammonium the reaction must be alkaline.

The splitting-up of sugars is usually attended with the formation of acetic, lactic, and butyric acids. In addition to these common acids, the energy of micro-organisms also leads to the formation of formic, propionic, baldrianic, palmitic, margaric, and other acids.

Sometimes the primary and secondary operations of bacteria differ in reaction. Thus, Bacillus diphtheriæ, when growing in bouillon, produces acidity during the first few days of active growth, but later an alkalinity which neutralizes and then replaces the acid. Such behavior probably depends upon the fact that the bacillus lives at the two periods upon different substances in the culture medium—in the primary period upon the sugars in the bouillon; during the subsequent period, upon the albumoses.

The varying behavior of micro-organisms in the body may in some cases depend upon varying conditions, by which the operations of a micro-organism differ at one time from those at another time.

Nitrogen Combinations.—Among the interesting phenomena of micro-organismal growth are those which have to do with nitrogen and its compounds. These are of chief interest to horticulturists, but of comparatively little importance to physicians. It is largely through the activity of bacteria growing about their roots that the leguminous plants are able to absorb and combine nitrogen. Other bacteria are useful to plants in that they reduce complex nitrogen compounds to nitrogen and ammonia.

Enzymes.—The formation of enzymes is one of the most important phenomena of micro-organismal life, as it is largely by these bodies that familiar effects are produced. Probably the most familiar example that can be cited is the curdling ferment by which many bacteria cause clotting of milk. An equally familiar example to every one acquainted with the methods of bacteriologic investigation is the liquefaction of gelatin and blood serum by proteolytic ferments produced by many forms of micro-organisms. Probably the diphtheria bacillus and the pneumococcus produce a fibrin ferment by which the fibrin is precipitated from the inflammatory exudates. The streptococcus may also produce smaller quantities of the same. Bacteriolytic enzymes are also produced by which the bacteria may themselves become dissolved or digested when dead.

The part which enzymes may play in disease is not yet clear, but may be important.

Toxins and Toxalbumins.—Toxins and toxalbumins are metabolic products of the pathogenic bacteria, and the disease-producing power of bacteria depends chiefly upon these products. They differ from the ptomains in that they are not the result of changes in the substratum, but are formed within the bacteria by metabolic processes and discharged into the surrounding media, and though grown in non-albuminous culture media, the micro-organisms are still able to form these products.

Toxins differ from toxalbumins in that although proteid substances, they fail to yield any of the albumin reactions. The greater number of toxic products are toxalbumins. Unfortunately, it has become customary to use the term toxin to indicate any poisonous substance produced by bacteria, but at present the term is being restricted to those poisonous substances devoid of albumin reactions. Of these, two, diphtheria toxin and tetanus toxin, are well known. Both substances are extremely active. They can be precipitated with ammonium sulphate and certain other salts, but cannot subsequently be obtained free from them. In general they are unstable in composition and readily change into toxoids on exposure to warmth, light, and oxygen. In the precipitated form they keep much better than in solution. They are completely destroyed by heating to 60° C. for a short time.

The toxalbumins are feebler poisons than the toxins, and are better known to us through their effects upon the diseased animals than from laboratory experiments. The poisons specific for cholera, typhoid fever, and other diseases are believed to be toxalbumins, and from the blood, vomit, and secretions of investigated cases of these diseases toxalbumins have been separated, although in cultures of the specific organisms they are present in almost inappreciable amounts.

Pathogenesis.—Bacteria, like other fungi, may be *pathogenic* or *non-pathogenic.*

The activities by which bacteria lead to disease productions are synoptized by Kruse as follows:

1. The organism cannot take on unrestricted growth in the body, and a local lesion results:
(*a*) Upon the surface, causing furuncles, etc. (staphylococci).
(*b*) Upon the surface, with extension by contiguity of tissue (erysipelas and phlegmons caused by streptococci).
(*c*) Surface growths with marked toxin production and distribution (diphtheria and tetanus).
(*d*) Deep focal inflammations (tubercles, etc.).
2. The organism is able to take on unrestricted growth in the body:
(*a*) By continuous extension, as in glanders.
(*b*) By metastasis, as in pyemia.
(*c*) By universal rapid growth and invasion, as in sepsis and anthrax.

The entrance of pathogenic bacteria into the body and the phenomena attending their reception there, together with the conditions favorable or unfavorable for their development and pathogenesis, constitute the subject matter best discussed under the captions Infection and Immunity.

THE ANIMAL PARASITES.

The numerous families and orders among which the animal parasites are distributed, together with the fact that there is a very small representation in each, makes it somewhat unsatisfactory to consider them from a zoölogic standpoint, yet the attempt to arrange them according to their harmful or harmless effects upon the host, or according to the source from which they are derived, is, if anything, less satisfactory.

The important animal parasites may be synoptized as follows:

I. **Protozoa**—
  Amœba coli.
  Amœba dysenteriæ.
  Cercomonas intestinalis.
  Cercomonas coli hominis.
  Trichomonas vaginalis.
  Trichomonas intestinalis.
  Megastoma entericum.
  Balantidium coli.
  Coccidium oviforme.
  Plasmodium malariæ.
  Pyrosoma bigeminum.
  Pyrosoma hominis.
  Trypanosoma lewisii.
  Trypanosoma brucei.
  Trypanosoma evansi.
  Trypanosoma gambensi.
  Trypanosoma theileri.
  Trypanosoma rougeti.
  Trypanosoma equinum.
II. **Vermes**—
  CESTODES—Tænia solium.
    Tænia saginata.
    Tænia cucumerina.
    Tænia nana.
    Tænia echinococcus.
    Bothriocephalus latus.
    Bothriocephalus cordatus.
    Bothriocephalus cristatus.
    Bothriocephalus liguloides.
  TREMATODES—Distoma hepaticum.
    Distoma lanceolatum.
    Distoma hæmatobium.
    Paragonimus westermanii.

NEMATODES—Ascaris lumbricoides.
Oxyuris vermicularis.
Eustrongylus gigas.
Filaria medinensis.
Filaria sanguinis hominis.
Uncinaria duodenale.
Uncinaria americana.
Trichina spiralis.
Trichocephalus dispar.
ARTHROPODA—Sarcoptes scabiæi.
Demodex folliculorum.
Pediculi.
Cimex.
Pulex.

An etiologic classification that may be of some advantage, though it is based upon no scientific basis, is as follows:

1. Parasites derived from other animals or individuals by contact and association:
    - Sarcoptes.
    - Pediculi.
    - Cimex.
    - Pulex.
    - Trypanosoma.
2. Parasites which enter man through the bites of insects (mosquitoes):
    - Plasmodium malariæ.
    - Filaria sanguinis hominis.
    - Trypanosoma.
3. Parasites derived from the soil in which the eggs or embryos are deposited:
    - Ascaris lumbricoides.
    - Oxyuris vermicularis.
    - Tænia echinococcus.
    - Coccidium oviforme.
    - Uncinaria.
4. Parasites derived from polluted water:
    - Amœba coli and Amœba dysenteriæ.
    - Uncinaria duodenale.
    - Distoma hepaticum.
    - Distoma lanceolatum.
    - Distoma hæmatobium.
    - Filaria medinensis.
    - Paragonimus (?).
5. Parasites derived from the flesh of other animals in which the embryo or eggs are contained:
    - Tænia solium.
    - Tænia saginata.
    - Tænia cucumerina.
    - Tænia nana.
    - Bothriocephalus latus.
    - Paragonimus westermanii (?).

It is difficult to separate the parasites into harmful and harmless forms, as many which do no harm as a rule sometimes cause suffering and death.

I. *Usually harmless parasites—*
    Amœba coli.
    Cercomonas intestinalis.
    Trichomonas intestinalis.
    Trichomonas vaginalis.
    Megastoma entericum.
    Balantidium coli.
    Ascaris lumbricoides.
    Oxyuris vermicularis.
    Trichocephalus dispar.
    Demodex folliculorum.
II. *Harmful parasites—*
    Tænia solium.
    Tænia saginata.
    Tænia cucumerina.
    Tænia nana.
    Distoma hepaticum.
    Distoma lanceolatum.
    Distoma hæmatobium.

Ascaris lumbricoides (when migratory).
Filaria sanguinis hominis.
Anchylostoma duodenale.
Sarcoptes scabiæi.

III. *Dangerous parasites*—

Amœba dysenteriæ.
Plasmodium malariæ.
Bothriocephalus latus.
Filaria medinensis.
Trichina spiralis.
Tænia echinococcus.
Coccidium oviforme.
Paragonimus westermanii.
Trypanosoma.

The parasites selected for description are important because of—(1) Their frequency; (2) their danger; (3) their formidable size; (4) their numbers.

I. **Protozoan Parasites.**—The **Amœba coli** was first described by Lösch, and has since attained prominence because of its relation to dysentery. Whether or not it is of etiologic importance in dysentery seems uncertain. The work of Councilman and Lafleur has shown the constant presence of the organism in certain forms of dysentery, though the more recent work of Shiga and Flexner indicates that Bacillus dysenteriæ is the cause of the epidemic form of the disease. The fact that amebæ have been found in the normal human feces and in intestinal evacuations in diseases other than dysentery has raised the question of the significance of Amœba coli and led to the supposition that **Amœba coli communis** is a different organism from **Amœba coli dysenteriæ.** In the absence of definite information concerning the varying pathogenesis or even absolute pathogenesis of either species it seems well to suppose that there are two species—one harmless, the other connected in some way with the etiology of tropical (amebic) dysentery.

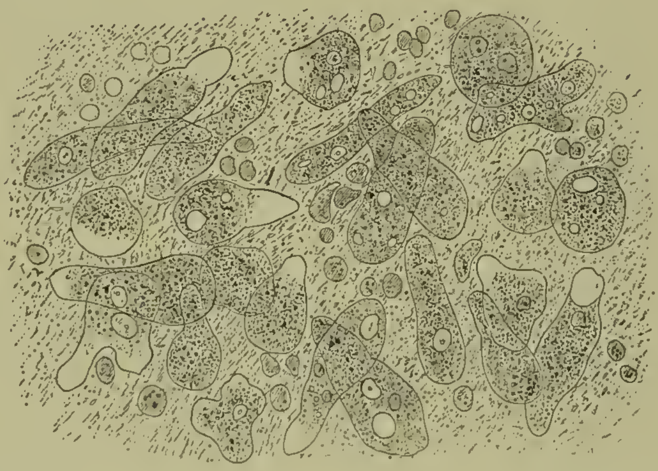

FIG. 123.—Amœba coli in intestinal mucus, with blood corpuscles and bacteria (Lösch).

The organisms are supposed to enter human beings through polluted water. They are from 20 to 30 μ in diameter, elongated or rounded in form, with elongate blunt pseudopods. They have no distinct cell membrane: each has a large pale nucleus and several vacuoles. When taken from dysenteric stools, they commonly contain blood corpuscles. Encysted forms also occur.

Attempts to cultivate the organism have failed, and all the inoculation experiments of necessity made with material containing amebæ and numerous bacteria as well, so that no correct conclusions can be drawn from them. In countries where dysentery is frequent the precaution of boiling the drinking-water guards against infection.

The **Coccidium oviforme,** a sporozoan parasite of elliptic shape, is a rare intestinal and hepatic parasite in man, although a common one in rabbits and mice. Human beings become infected through association with infected animals from whose intestines the parasites are discharged.

The organism makes its first appearance as a minute, granular, globular body in the interior of one of the columnar epithelial cells of the intestine or bile-ducts, slowly increasing in size until it greatly exceeds the size of the cellular host, making it appear like an exaggerated goblet cell. The further development occurs in one or the other of two ways: either the full-grown parasite undergoes segmentation into a multitude of small falciform embryos which immediately enter new epithelial cells in the neighborhood and so keep up the infection, or become surrounded by a dense double capsule, and, thus encysted, pass into the intestine with the bile and escape with the feces. Delepine has shown that the encysted parasites are not at once able to infect fresh animals to which they may be fed, but require to undergo a series of changes outside of the animal body in soil.

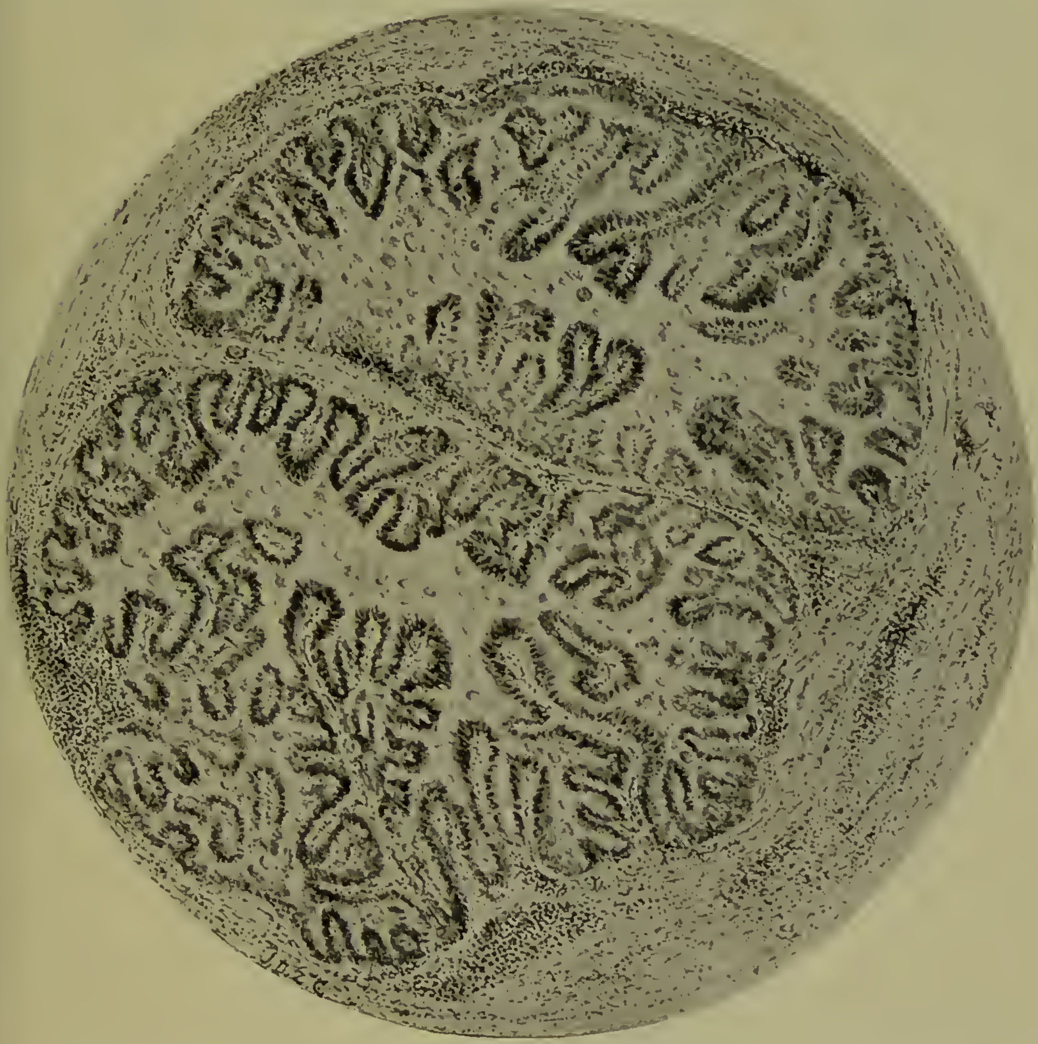

FIG. 124.—Coccidiosis of rabbit's liver. Section of one of the affected bile-ducts, showing the papillary outgrowths from the mucous membrane and the signs of inflammation in the surrounding tissue.

The encysted parasite is oval or elliptic, somewhat flattened, and has a distinct double capsule, which contains a granular body with what seems to be a small nucleus. When kept moist for some time, the granular contents assumes a spheric shape, retracting from the capsule and leaving a surrounding clear space, divides twice with the formation of four embryos, in each of which two falciform spores are developed. Infection is possible, and when ripe coccidia, the embryos, or the spores are taken into the stomach upon fresh vegetables, in polluted water, or are carried into the mouth in dust or by soiled fingers, the gastric juice dissolves away the spore capsules, liberating them in the form of ameboid embryos which readily infect the cells.

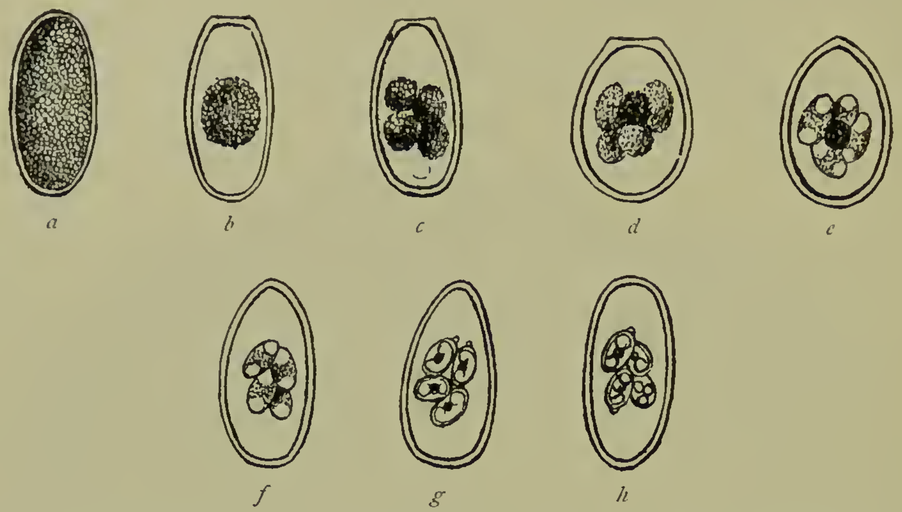

FIG. 125.—External cycle of developments of the Coccidium oviforme, (*a* to *g*) showing the division of the cytoplasm into four spores, each of which contains two falciform embryos (*h*). This cycle of development occurs in damp soil outside of the animal body.

Space does not permit us to enter into a description of the lesions caused by the Coccidium oviforme, but they are often so extensive and serious as to cause death in rabbits and in feeble human beings. They consist of chronic proliferative and obstructive affections of the bile-ducts, and terminate in the formation of parasitic cysts in the liver.

The prophylaxis is clear. Precautions should be taken to avoid retaining among domestic animals those infected with the disease. In handling infected animals or their discharges precautions should be taken to disinfect the hands, etc. The soil of infected rabbit warrens should be disinfected with lime and the infected rabbits killed off.

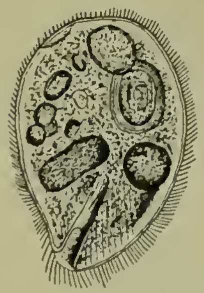

FIG. 126.—Balantidium coli (Mamsten).

The **Balantidium** or **Paramœcium coli** is a rounded, unicellular organism measuring from 7 to 10 μ in length. It is surrounded with short cilia, which enable it to swim with a rapid darting movement. At one end, which is usually more pointed than the other, there is a mouth orifice about which the cilia are longer. A nucleus, numerous vacuoles, and a miscellaneous collection of food particles can be made out in the cytoplasm. The two largest vacuoles are usually contractile.

It is said that this organism is habitually present in the intestine of hogs and occasionally present in man. Diarrheal troubles have been referred to its presence.

The **Cercomonas intestinalis** is a peculiar organism of a shape suggesting a large spermatozoön with a short tail. It measures from 10 to 12 μ in length, and is made up of a pear-shaped body from the blunt end of which a single undulating flagellum projects. It has been observed in a large number of intestinal diseases, but probably has no significance.

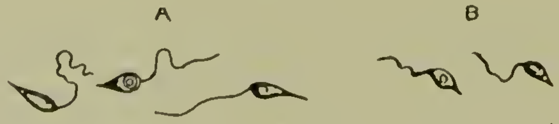

FIG. 127.—Cercomonas intestinalis: *A*, Larger, *B*, smaller, variety (Davaine).

The **Cercomonas coli hominis** was described by May, who found it in the intestine of a case of carcinoma of the stomach. It is of spindle shape, and has four flagella attached to one end. It is not known to be of pathologic importance.

The **Trichomonas vaginalis** is an elongate, oval parasite measuring about 10 μ in length. From the anterior end three whip-like flagella project. From the base of their attachment to about the center of the body an undulating membrane is attached. This is occasionally provided with five or six small cilia. The body substance is usually finely granular, colorless, and apparently without a nucleus. The organism is actively motile, through the agency of the flagella. It was found by Hausmann in about 40 per cent. of pregnant and non-pregnant women, but it is probable that it never occurs in normal vaginal secretions. It is most numerous when the secretions are strongly acid. Dock has found the organism in human urine.

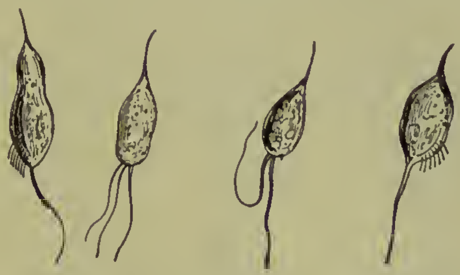

FIG. 128.—Trichomonas vaginalis (after Kölliker and Scanzoni).

It is very uncertain whether the trichomonas has any pathologic significance.

The **Trichomonas intestinalis** is a slightly larger organism, measuring about from 10 to 15 μ x 7 μ. The anterior end is more blunt than in the other species, and the tail is sharper. The undulating membrane is larger and has from 10 to 12 cilia. There are usually four flagella (Grassi). It is improbable that it is of pathogenic importance.

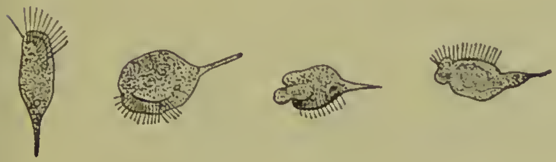

FIG. 129.—Trichomonas intestinalis (after Zenker).

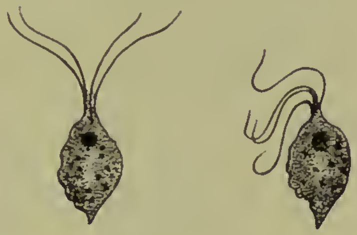

FIG. 130.—Cercomonas coli (after May).

Megastoma entericum is a common parasite of the intestine of the mouse and an occasional parasite of man. It measures from 10 to 16 μ in length by 5 to 7.5 μ in breadth. It has an irregular pear shape and a peculiar excavation situated obliquely near the broad anterior end. From the anterior edge of this depression two long flagella arise, while from its inferior or posterior edge a group of four flagella arise. The front end of the organism is blunt and rounded, the posterior end sharply pointed and provided with a pair of flagella. Two nuclei are situated near the blunt end. A delicate capsule surrounds the finely granular cytoplasm. When free, the organism is capable of rapid movements. As a parasite of the intestine, how-

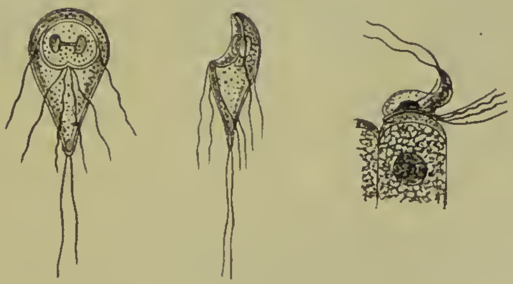

FIG. 131.—Megastoma entericum (after Grassi and Schewiakoff).

ever, it probably lives by absorbing nourishment from epithelial cells, to which it attaches itself by its concave depression. The organism is probably harmless.

Plasmodium malariæ, Hæmamœba malariæ, or **Hæmatophyllum malariæ** is a parasite of great importance with which human beings become infected through the bites of infected mosquitoes. At the time such a mosquito bites small filiform embryos of this parasite escaping from the cells of the salivary glands enter with the proboscis wound and cause the infection. According to Robert Koch, there are five true malarial parasites:

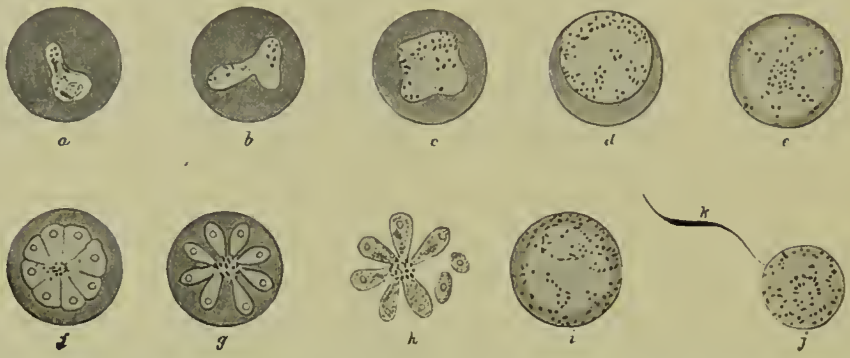

FIG. 132.—Parasite of quartan malarial fever: *a, b, c, d,* Enlarging intracellular parasites; *e, f, g, h,* segmentating parasites forming a distinct roset from which the spores separate; *i,* macrogametocyte; *j,* microgametocyte; *k,* flagellum.

1. The parasite of tertian fever.
2. The parasite of quartan fever.
3. The Halteridium Danilewskyi (of birds).

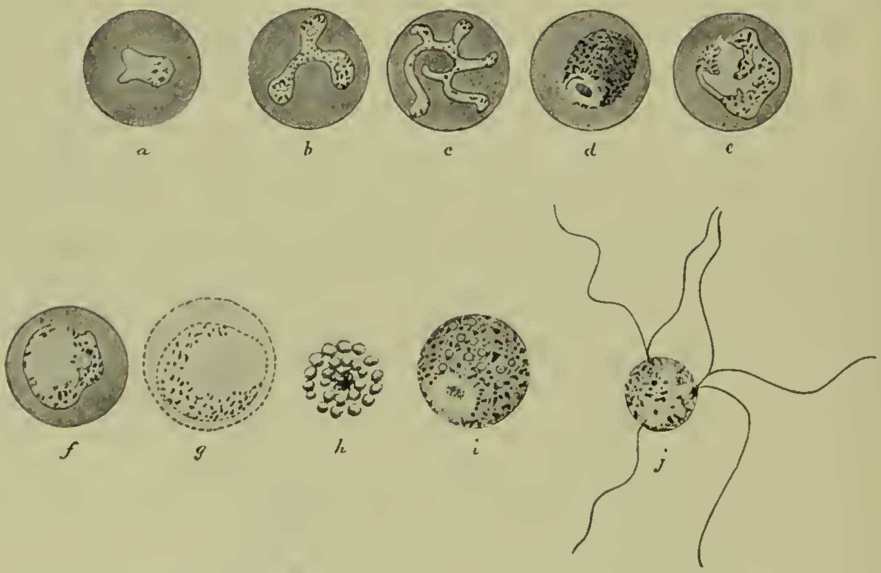

FIG. 133.—Parasite of tertian malarial fever: *a, b, c, d, e, f, g,* Growing pigmented parasite in the red blood corpuscles; *h,* spores formed by segmentation of the parasite—no roset is found, but concentric rings of the cytoplasm divide; *i,* macrogametocyte; *j,* microgametocyte with flagella.

4. The Proteosoma Grassii (of birds).
5. The parasite of monkeys, discovered by Kossel in Africa.

The life history of these parasites is probably similar, but the intermediate and definitive hosts probably differ in all.

The entrance of the "blasts" or embryos by the puncture made by the proboscis of the mosquito is followed by the infection of red blood corpuscles to which the embryo at first adheres, and into which it subsequently enters. The appearance of both human parasites (tertian and quartan) is identical at first, each appearing as a small hyaline body of irregular shape. This body slowly enlarges, becoming distinctly ring-shaped in the tertian form. It soon contains pigment from destruction of the corpuscle upon which it preys, which appears in the form of irregular black particles. The parasites are ameboid, and constantly change their form, the pigment granules flowing this way and that way with the cytoplasmic currents. A greater number of pigment granules appear in the tertian parasites, though the granules are larger in the quartan parasites.

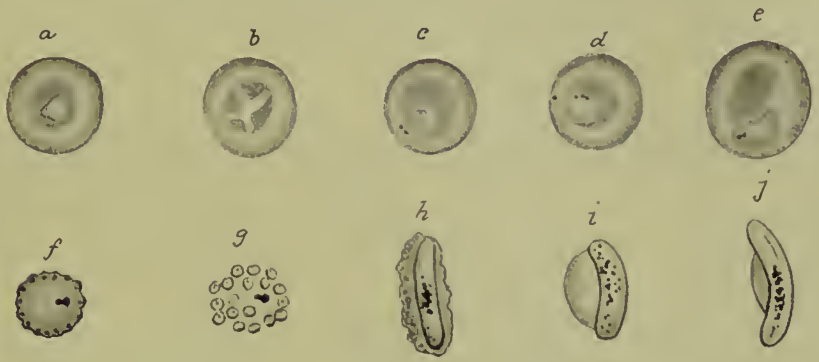

FIG. 134.—Parasite of estivo-autumnal fever: *a*, *b*, *c*, ring-like and cross-like hyaline forms; *d*, *e*, pigmented forms; *f*, *g*, segmentary forms; *h*, *i*, *j*, crescents.

The two parasites resemble each other until almost as large as a red blood corpuscle, when the quartan parasite ceases to grow and proceeds to sporulate. The pigment granules that have been distributed irregularly over the surface now pass to the center, and the cytoplasm divides into eight or ten divisions, the lines of cleavage descending from the surface of the parasite to its center. This cleavage soon progresses until a perfect roset is formed, the pigment granules in the center, the whole still surrounded by the shell of the former blood corpuscle. With the final disintegration of the corpuscle the segments of the parasite fall apart, and eight spores or embryos are liberated, ready to infect new corpuscles. From the time of the first infection to the sporulation of the quartan parasite the interval is seventy-two hours.

The tertian parasite behaves somewhat differently and increases in size until it is considerably larger than an erythrocyte, when it undergoes a less regular cleavage into from 18 to 20 spores, without the roset formation. These spores similarly penetrate new corpuscles and begin the developmental cycle again. The entire period between the infection of the corpuscles by the embryo parasites and the perfect development and final segmentation of these is, in the tertian parasite, forty-eight hours.

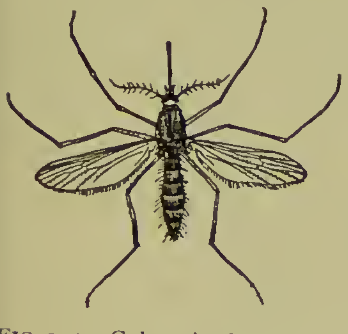

FIG. 135.—Culex, the host of the filaria.

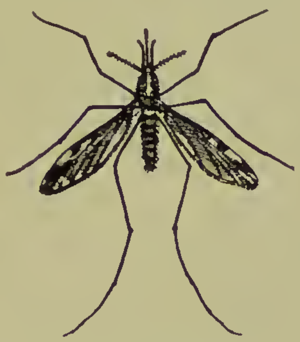

FIG. 136.—Anopheles, the host of the malarial organism.

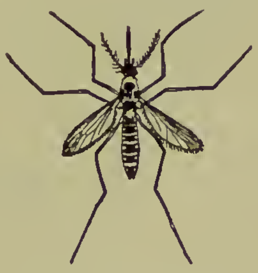

FIG. 137.—Stegomyia, the host of the yellow-fever parasite.

The earlier writers described a *quotidian parasite* which appeared sometimes in a pigmented, sometimes as a non-pigmented, form. It is not now recognized, quotidian forms of malaria being regarded as a double infection with the tertian parasite, or a multiple infection with the quartan parasite.

The *estivo-autumnal* form of malaria, characterized by its severity and by the large number of parasites in the blood, among which are numerous peculiar *crescentic bodies*, is probably a variety of tertian infection.

The developmental cycle described is complete in the human host, but there is another cycle by which the infection is originally brought to man.

Koch mentions three discoveries which have perfected our knowledge of the malarial parasite: (1) The discovery of the parasite by Laveran; (2) the discovery of its developmental cycle in man by Golgi, and (3) the discovery of its developmental cycle in the mosquito by Ross.

The mosquitos that propagate malaria are not the common *culex*, which swarm everywhere over all the world, but a larger, and in most cases rarer, genus, *Anopheles*.

Before following the parasite in the mosquito, however, it will be necessary to speak of certain peculiar forms that the parasite assumes in the blood of man, and that have nothing to do with the life cycle described. The most noticeable of these is the crescentic body of the estivo-autumnal fever. It is an elongate, slightly curved, crescentic body, with a collection of pigment near the center. The nature of these bodies puzzled observers, and it is only recently that they have been recognized as the *gametocytes*. Crescents occur rarely in tertian fever, and only in the pernicious form, but large rounded bodies analogous to them are commonly found. Of these, one is large and has a clear substance; the other is smaller and has a more granular substance. From the latter peculiar filaments are sometimes given off, forming what have been described since the time of Laveran as "*flagellated bodies*." If the blood containing these parasites is kept moist for a time and frequently examined under the microscope, the cytoplasm of the granular organism may be seen suddenly to become tumultuous, and extend elongate filaments with energetic lashing movement. These remain attached for a few moments, then break loose, swim away, and disappear. These were for a long time supposed to be some kind of degeneration of the parasite, but MacCallum, in following one of the flagella of Halteridium danelewskyi, found that it, together with other similar bodies, advanced toward one of the large hyaline bodies, and ultimately formed a symbiosis with it. The same fact was subsequently determined for the tertian malarial parasite. This symbiosis is undoubtedly a form of sexual fertilization. The large hyaline bodies are, therefore, described as *macro-gametocytes*, the flagella as *micro-gametocytes*, and the office of the large globular forms of tertian fever and the crescents of the estivo-autumnal fever made clear. The fertilized parasite is called a *zygote* or *zygocyte*. Ross found that the sexual symbiosis took place in the stomach of the mosquito, and having with much labor determined that the *anopheles* were the proper hosts of

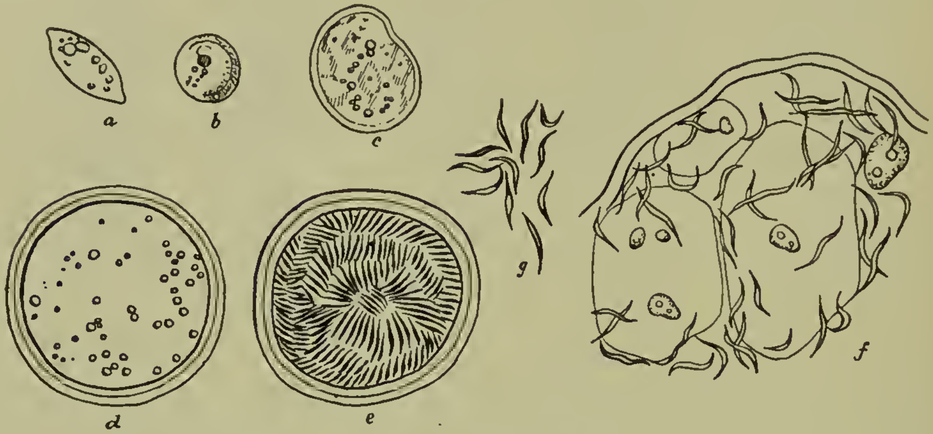

FIG. 138.—Developmental cycle of the malarial parasite in the mosquito: *a*, *b*, *c*, Zygocytes; *d*, *e*, meres with contained blasts; *g*, free blasts; *f*, blasts migrating into the salivary gland-cells (from Manson).

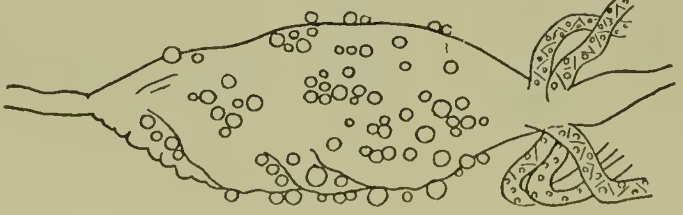

FIG. 139.—Stomach of mosquito with zygocytes on the outer surface.

the parasite, discovered that the zygocytes penetrate the wall of the stomach or mid-intestine of the mosquito, and remain attached to its outer wall as pigmented protoplasmic bodies, continuing to grow until many times the original size is attained. They next undergo division into a dozen or more rounded bodies called *meres*, each of which finally undergoes a complete cleavage into a multitude of small filamentous or vermicular spindles, known as *blasts*. With the formation of the blasts the zygocyte ceases to exist, and these minute embryo parasites escape free into the body cavity of the insect, making their way to all parts of it, but apparently tending toward the salivary glands, with whose secretion they are eliminated. It is thus seen that in the act of biting the mosquito introduces into its victim a number of the embryo parasites with its saliva. If, however, the mosquito is not infected and no blasts are in the saliva, no infection follows its bite. The blasts, once in the human blood, attack the corpuscles and begin the cycle of development already described as characteristic of the organism in man. It thus appears that the mosquito is the definitive host of the parasite, and man only the intermediate host.

The peculiar life-history of the parasite having been established by independent workers in different countries, has been confirmed over all the world, and at the present time there is scarcely a parasitic affection about which we have more positive and correct information.

Malarial fever is acquired, so far as we are informed at present, solely from the bites of the mosquitos of the genus Anopheles, and it is only where these mosquitos exist that there is danger of infection. The bite of the anopheles is, however, in itself as harmless as the bite of the commom culex except when it is already infected by some human being suffering from malaria. Having thus become infected, the mosquito becomes dangerous from the time the blasts make their appearance in the saliva, which, according to the temperature, varies from eight to fourteen days. Once thus infected, a mosquito remains dangerous throughout the remainder of its life, and can infect a number of human beings in a single night by biting them. Correspondingly, a single human being may infect any number of mosquitos that prey upon him in a single night, and leave behind him in a place formerly free of malaria a host of infected insects capable of spreading malaria fever.

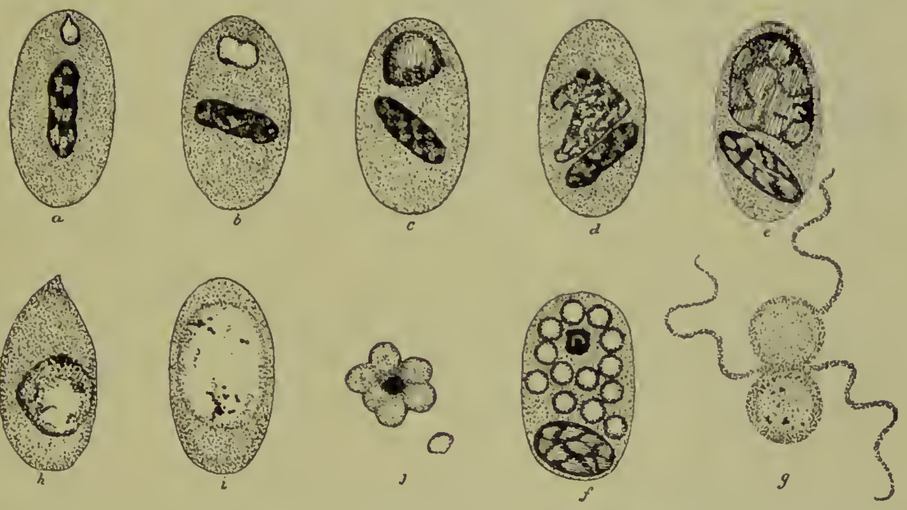

FIG. 140.—Proteosoma Grassii, the malarial parasite of small birds: *a, b, c, d, e*, Growing parasite in the red blood corpuscle (in its growth the parasite displaces the nuclei of the corpuscles); *f*, segmenting parasite; *j*, abnormal segmentation; *g*, gametocytes with flagella, apparently conjugating; *h, i*, abnormal parasites (modified from Opie).

Concerning the prophylaxis of the disease, Robert Koch suggests that all who enter malarious districts and are in danger of infection keep themselves protected by the use of quinin, and that the systematic use of quinin among cases of malaria, by destroying the parasites in the circulating blood, will prevent the infection of new mosquitos and so limit the spread of the disease and probably finally exterminate it.

The extermination of the anopheles mosquitos is an almost hopeless task, as they are abundant, multiply vigorously, live in very small quantities of water, and have a very short embryonal life. Something can be achieved by the use of kerosene, which, when poured upon the surface of ponds or puddles so as to make a film upon the surface, prevents the "wigglers" or embryo mosquitos from breathing. Draining and filling up the puddles, ponds, and swamps are excellent expedients. The importation and multiplication of dragon-flies are scarcely useful, as the latter are diurnal insects, while the anopheles are purely nocturnal.

In the absence of satisfactory means for ridding an infected district of the mosquitos, the one thing to be done is to protect ourselves from the mosquitos, and the work done by the field commissions in Italy, both by the Italians and by the English, shows positively that the most malarious districts in the world are harmless if sufficient precautions are taken to guard against mosquitos. Mosquito-netting in all the windows and canopies of netting over the beds will do more good than any other means for the prevention of malaria.

The anopheles mosquitos are nocturnal, and are very rarely seen in the daytime, hence the danger of infection is at night. They usually fly low, so that the danger of infection is greater upon or near the ground than at some altitude, as the upper stories of buildings or upon hills. They fly by preference in still, dry weather, rather than in a stiff breeze, hence the hot still nights of summer are more dangerous than the windy ones. The insects frequently hibernate in houses and in warmed rooms, and may bite during the winter, so that infection of human beings is by no means limited to the summer or to warm weather, though during the warm weather, because of the greater number of mosquitos, the frequency and danger of infection are greater than at any other time of the year.

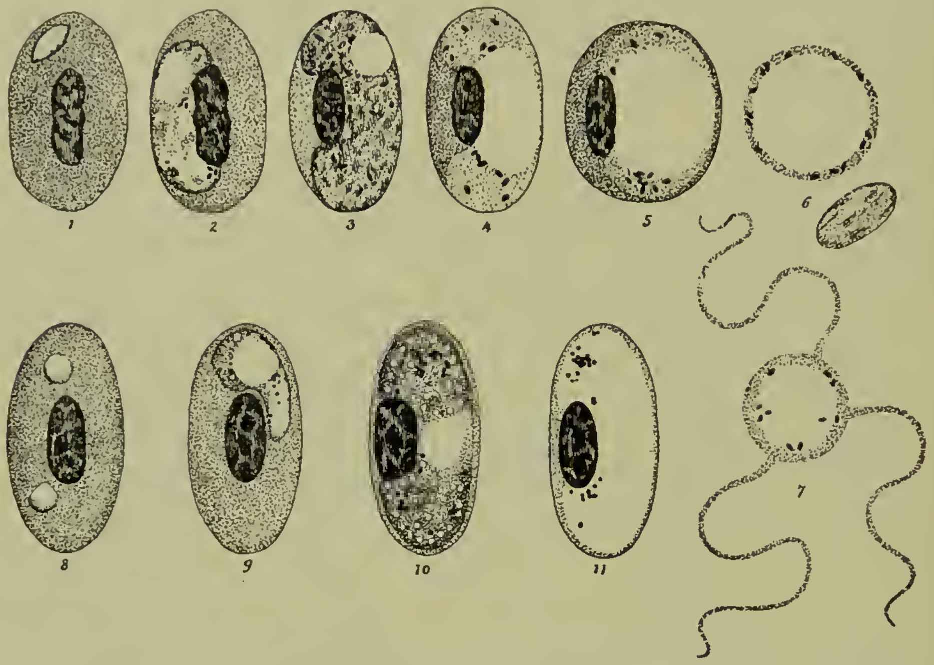

FIG. 141.—Halteridium Danilewskyi, the malarial parasite of large birds: *1, 2, 3, 4, 5,* Showing handle-shaped parasites in red blood corpuscles; *6,* macrogametocyte, the nucleus of the corpuscle extended; *7,* microgametocyte with flagella; *8, 9, 10, 11,* atypical forms of the parasite (modified from Opie).

Yellow fever is now known to be a parasitic disease, probably caused by a protozoan organism. The parasite is not known, but it has been demonstrated that a mosquito known as Stegomyia fasciata is the definitive host.

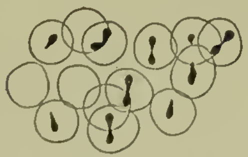

FIG. 142.—Pyrosoma bigeminum.

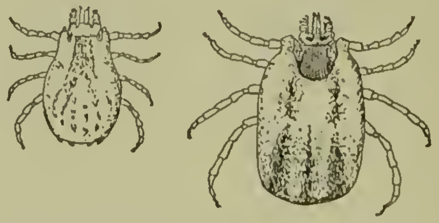

FIG. 143.—Boöphilus bovis: the Texas fever tick.

Pyrosoma bigeminum (Smith) is the parasite of *Texas fever,* an acute and occasionally chronic febrile affection of cattle, for the most part confined to warm climates. The organism is known only as it appears in the blood of the infected animals, where it occurs as an intracellular parasite of the red blood corpuscles. It is very small and of a pyriform shape.

The careful researches of Smith and Kilbourne have shown that the definitive host of the parasite is the common cattle-tick of the South, the Boöphilus bovis. The tick takes the parasite into its body with the blood of its host, but the developmental stages it undergoes in the tick are unknown. It is, however, peculiar in that it passes into the eggs of the tick and infects the newly habited embryos so that these have the power of imparting Texas fever to cattle.

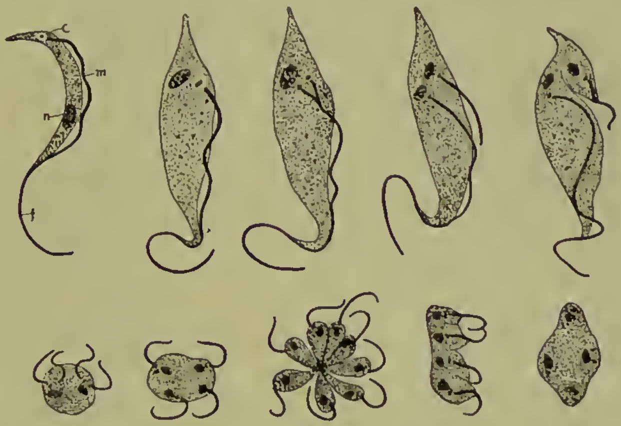

FIG. 144.—Trypanosoma, showing multiplication by division (from Laveran): *n*, Nucleus; *c*, centrosome; *m*, undulating membrane; *f*, flagellum.

A pyrosoma (Pyrosoma hominis) also causes "tick fever" of man.

Trypanosomiasis.—Trypanosomes have been known for some time as blood-parasites of rats and have attracted considerable attention because of their etiologic importance in "nagana," or Tse-tse fly disease, a common and pestilential epidemic disease of cattle in parts of South Africa, and "surra" or "mal de Caderas," a similar affection of horses, common in Asia and South America. Trypanosomes are also known to be the cause of "dourine" or the "maladie de coit" of horses, and recent investigations have shown the presence of a trypanosome in the cerebrospinal fluid in cases of African lethargy or "sleeping sickness" and in febrile affections of human beings exposed to the bites of the Tse-tse fly.

The **trypanosomes** are of spindle shape, longer than the diameter of a red blood cell, pointed at each end, the posterior end terminating in a long flagellum. Along one side of the body an undulating membrane is attached. A nucleus and a centrosome can usually be discerned. The organisms multiply sometimes by longitudinal cleavage, sometimes by roset formation.

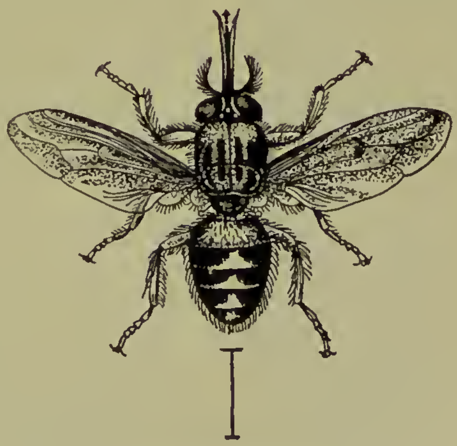

FIG. 145.—Glossina morsitans, or Tse-tse fly.

These parasites, with the exception of that causing dourine, which is transmitted by coitus, require definitive and intermediate hosts. The definitive host of nagana is known to be the Tse-tse fly or Glossina morsitans, and that of sleeping sickness, the Glossina palpalis. The parasite of surra is also a fly, probably Stomoxys calcitrans.

II. **Worms.**—A. CESTODES.—The worms of this group comprehend the well-known tape-worms. They may be large or small, but are all characterized by a flattened, elongate form, segmented body, the presence of suckers, and sometimes hooklets by which to attach themselves, and by the absence of an alimentary apparatus. Nearly all these worms have a complicated life-cycle requiring two hosts for its completion. They are all hermaphroditic.

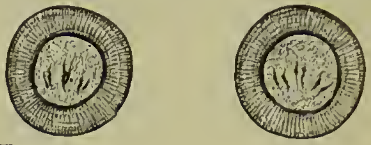
FIG. 147.—Eggs of Tænia saginata.

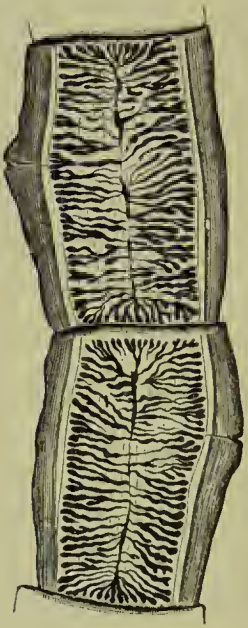
FIG. 148.—Mature segments of Tænia saginata.

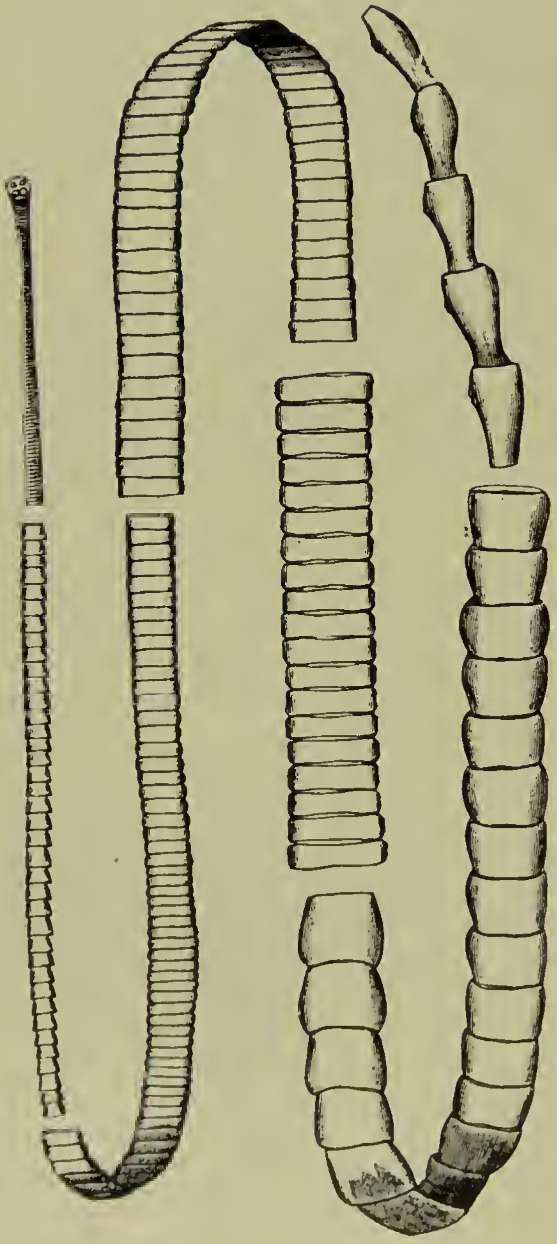
FIG. 146.—Tænia saginata (Eichhorst).

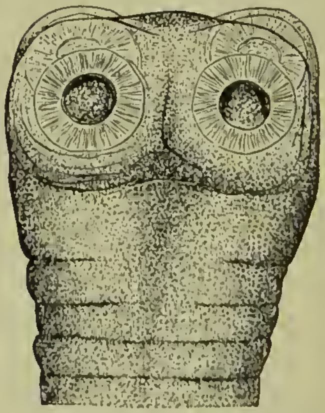
FIG. 149.—Head of Tænia saginata (Mosler and Peiper).

The adult worm is known as a *strobile*. It consists of a small head, short, usually narrow neck, and a series of segments or *proglottides* varying from three in Tænia echinococcus to thousands in Bothriocephalus latus. Each proglottis is in itself a complete sexual animal and contains a large, usually branched uterus, which receives myriads of eggs from the ovaries, and testicular structures with vasa deferentia. The sexual opening is sometimes at the side of the proglottis (tenia), more rarely at its inferior edge (bothriocephalus). Each segment when ripe contains thousands of eggs. The ripe segments detach one by one as the worm grows, and though myriads of eggs escape from the segments into the feces, large numbers still remain in the segments passed with them. The eggs eaten by the appropriate host develop in his intestine into embryos, which migrate from that viscus to the voluntary muscles or other tissues, and there repose until the infected tissue is eaten by the other appropriate host, when the embryos not destroyed by cooking or comminuted by the teeth develop into strobila in the intestine. The embryo worm in the quiescent state in the tissues is known as a *scolex*, the cyst in which it is contained, a *cysticercus*.

Tænia mediocanellata, the beef tape-worm, or *saginata*, is the most common tape-worm in the United States. It is a large worm, measuring from 4 to 8 meters in length. The head is small, being only about 2 mm. broad. It is flattened at the top, and presents four rounded suckers upon the flattened area. There is no rostellum and there are no hooklets. The neck is short. The immature anterior proglottides are broader than long, the mature proglottides longer than broad. The worm is nearly white—a sort of a cream white—in color. Each mature proglottis is from 4 to 7 mm. broad and from 16 to 20 mm. long. The sexual opening of each proglottis is in the side, those of different segments usually alternating, first upon one side and then upon the other. Within the segment the uterus can usually be seen by the yellowish color imparted by the contained eggs. The uterus extends along the middle line of the segment, giving off branches on both sides. Some of the branches are themselves branched, but usually they are simply tubular and terminate in broad cecal pouches.

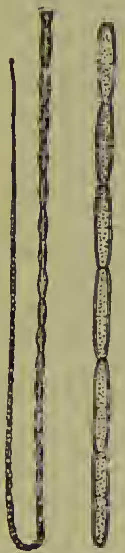

FIG. 150.—Tænia elliptica (Mosler and Peiper).

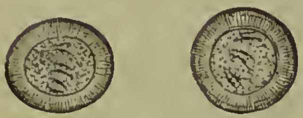

FIG. 151.—Eggs of Tænia elliptica.

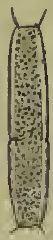

FIG. 152.—Mature segments of Tænia elliptica.

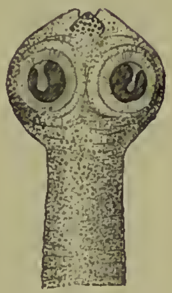

FIG. 153.—Head of Tænia elliptica.

The eggs, when ripe, measure 0.03 mm. in diameter, are ovoid in shape, and are surrounded by a thick shell that is radially striated and not infrequently shows one or two projecting tail-like processes. Within the ripe eggs four hooklets of the embryo can usually be observed.

The strobile of this worm lives in man, the scolex in cattle which become infected, doubtless from soil polluted with human feces. Man derives the scolex from improperly cooked meat. The worm is usually solitary in man, but several, and sometimes as many as forty, have been found in the same host. The cysticerci may also be numerous in the intermediate host.

When the eggs of this parasite are swallowed by man, they develop exactly as in the ox, and man himself becomes an intermediate host. Though many cases of embryo infection or *Cysticercus cellulosæ* occur among men, it is not known that the strobile ever develops in cattle.

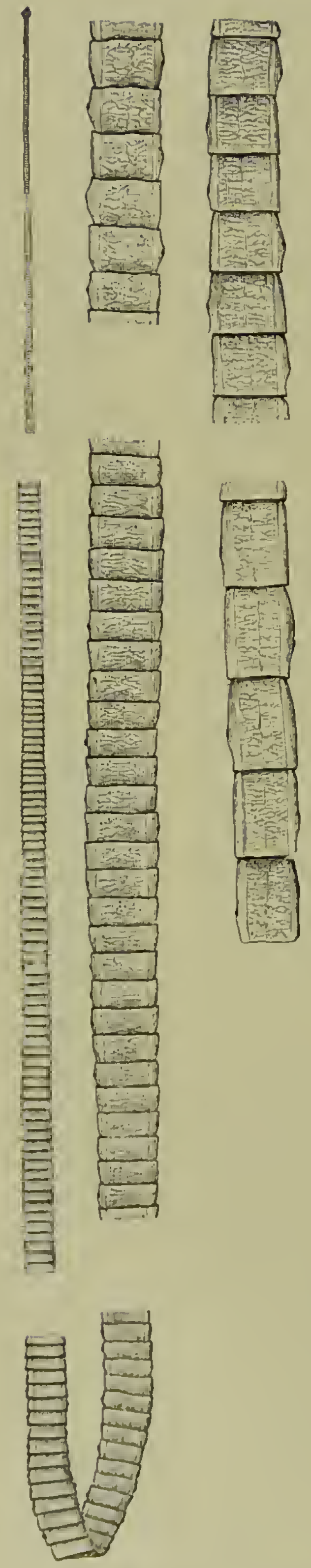

FIG. 154.—Tænia solium (Mosler and Peiper).

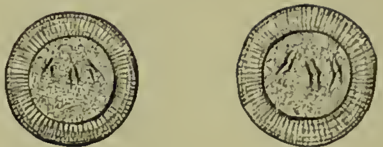

FIG. 155.—Eggs of Tænia solium.

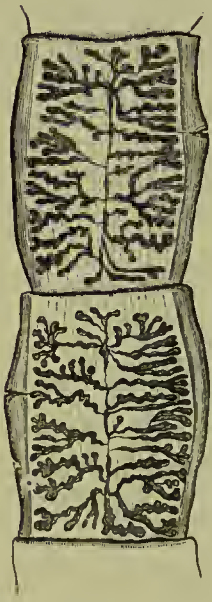

FIG. 156.—Mature segments of Tænia solium.

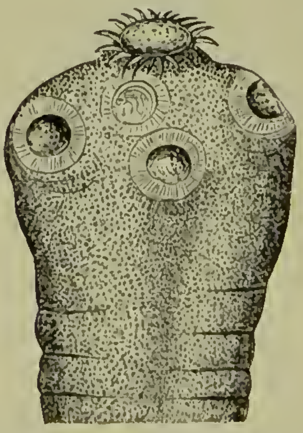

FIG. 157.—Head of Tænia solium (Mosler and Peiper).

this probably depending upon the fact that cattle, not being flesh eaters, have no opportunity to become infected.

The scolices of the cysticercus disease will be single or numerous, according as few or many eggs were swallowed. Usually there are few, and unless they happen to take up their encysted life in some peculiar position, as in the eye or brain, there is nothing to direct attention to them. When present in large numbers, they may cause distinct symptoms, and after death the little cysts are found in abundance. The cysticercus, when examined, may be recognized by its cystic form, and by the fact that there is invaginated in it a small body corresponding to the head of the tape-worm.

As ordinarily seen in man, the Tænia mediocanellata is a comparatively harmless parasite whose presence provokes no other disturbance than indefinite digestive and reflex symptoms.

Tænia solium, the pork tape-worm, is very rare in this country, though common in Europe. It is a smaller worm than the preceding, usually not longer than 2 or 3 meters. It has the same color and general appearance. The head, however, is quite different in that it is rounded in form with a projecting rostellum, armed, upon the summit, with from 30 to 40 hooklets and four lateral suckers. Hooklets and suckers seem solely for the purpose of attachment. The neck is about 1 cm. long and is followed by a long series of from 200 to 450 proglottides. The first of these are very narrow and elongate, but soon change, and hundreds of the lower segments are broader than long. The ripe segments, however, are much longer than broad.

FIG. 158.—Tænia nana, about natural size (Mosler and Peiper).

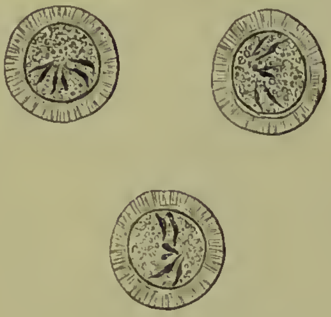

FIG. 159.—Eggs of Tænia nana (Mosler and Peiper).

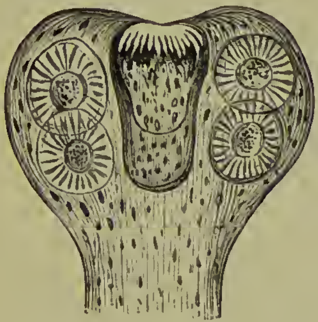

FIG. 160.—Head of Tænia nana (Mertens).

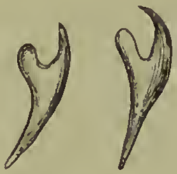

FIG. 161.—Hooks of Tænia nana (Mertens).

The sexual openings of the segments are situated laterally and alternate on the two sides. The uterus is of the same general appearance as that of the Tænia mediocanellata, but the lateral branches are frequently dendritic. When the dendritic appearance is well developed, it is usually characteristic of the species.

The eggs closely resemble in size and shape those of the other species, but are perhaps more globular.

The strobile inhabits the human intestine, the scolex occurring in the flesh of the hog. By swallowing the eggs man may become affected with the cysticercus disease—Cysticercus cellulosa.

Tænia elliptica sive cucumerina is the tape-worm of the cat and dog. It measures from 15 to 20 cm. in length, and is delicate and slender, being made up of elongate, elliptic segments. The head has a rhomboidal form, and is very small. It is provided with a rostellum, which can be projected and retracted, bearing about 60 small hooklets arranged in four rows. The strobile has a slightly reddish color from the presence of eggs in the segments. Each segment has a double genital apparatus with a sexual opening on each side.

The strobile inhabits the cat and dog. Sometimes numbers of them are present and cause intestinal irritation. The flea is supposed to be the intermediate host.

Through association with pet cats and dogs children between the ages of nine months and three years have been known to become infected by the parasite. Older children sometimes suffer; adults are very rarely affected.

Tænia nana is a minute tape-worm of about 2 to 3 cm. in length and 0.5 mm. in breadth. The source of the worm is unknown, though it is suspected that certain insects or snails may be the intermediate host. It is thought by Grassi that the worm can develop from eggs without any intermediate host. The head of the worm is rather peculiar. It has a rostellum that can be protruded or retracted, armed with from 22 to 27 hooklets. There are four suckers. The neck is very narrow. There are about 200 segments, all broader than long.

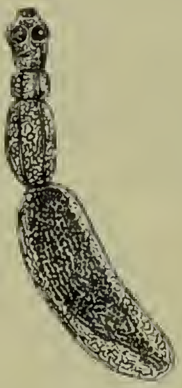

FIG. 162—Tænia echinococcus; enlarged (Mosler and Peiper).

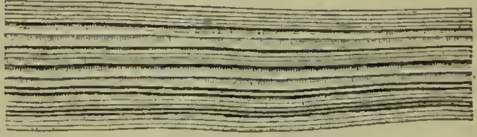

FIG. 163.—Cross-section through echinococcus membrane (Mosler and Peiper).

The worm lives in the small intestine, where it attaches itself by sinking its head for some distance into and below the mucous membrane. There may be a single worm or there may be thousands. It is a common parasite of dogs and cats, and not uncommon among children. The worms cause no definite symptoms.

Tænia Echinococcus.—The adult form of this worm is very small, the entire strobile not exceeding 4 or 5 millimeters in length, and consisting of only four segments. The head has a rostellum, armed with a circle of from 14 to 25 hooklets and 4 lateral suckers. Only the last segment is sexually perfect, containing a large uterus. The sexual opening is on the side of the segment. The eggs measure from 17 to 30 μ in diameter and are said to have very thin shells.

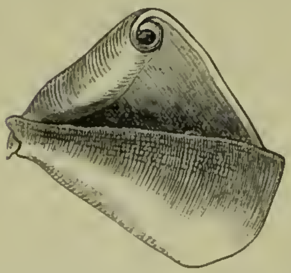

FIG. 164.—Echinococcus membrane with curled-in edges (Mosler and Peiper).

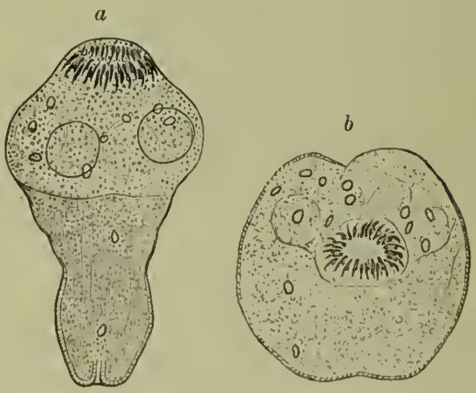

FIG. 165.—Head of echinococcus: *a*, Head protruded; *b*, head drawn in (Mosler and Peiper).

The strobile inhabits the dog and may be present in the intestine in large numbers. Man is the intermediate host, and is subject only to the cysticercus disease.

When the eggs are swallowed by man, the shells are digested by the gastro-intestinal juices and the embryo parasite set free. It does not remain in the intestine, but immediately migrates to the liver or elsewhere and becomes encysted. The cyst-wall becomes rather thick, has a bluish-white color, is brittle, and tends, when broken up, to roll together in an inverted form. The cyst-wall consists of two layers, an outer cuticular dense layer and an inner parenchymatous or granulocellular layer. The parenchymatous inner layer is of great importance in the subsequent changes. The embryo parasite or scolex develops into the cyst containing clear fluid, its own identity thus being obliterated. The cysts vary in size, and may become as large as a cocoanut. As the cyst increases and the parasite multiplies, the varying changes receive different names:

1. Echinococcus scoliciparicus.
2. Echinococcus hydatidosus.
3. Echinococcus multilocularis.

1. *Echinococcus scoliciparicus.*—As the original cyst increases in size little buds develop from the inner granulocellular layer of its wall. If these be carefully examined with the microscope, they are found to have hooklets and suckers, and are, in reality, embryo parasites. As these embryos increase in size they also become cystic, and from the walls of the little cysts new parasites develop which become inverted into the cysts. In this way a large number of new embryos is constantly developing as the old ones die. In the clear fluid of the cyst large numbers of the little hooklets of the dead worms are present, microscopic finding of which is diagnostic of the disease.

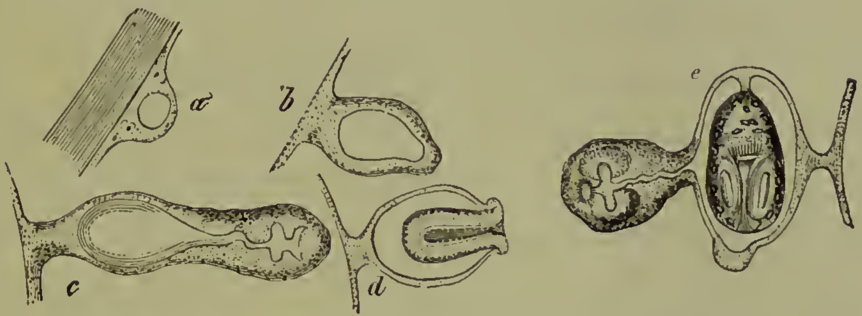

FIG. 166.—Development of ovum: *a*, Suspended heads; *b*, primary rudiment of head; *c*, further development; *d*, intussusception of head; *e*, later budding. × 90 (Leuckart).

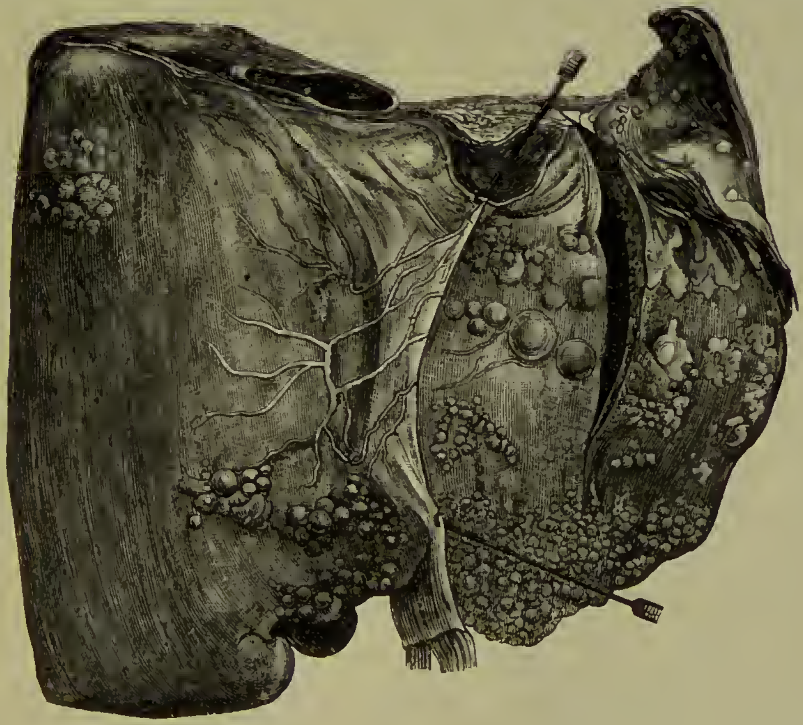

FIG. 167.—Multilocular echinococcus. Anterior view of left auricle of heart (Waldstein).

2. *Echinococcus hydatidosus.*—In this form well-developed cysts occur within the parent cyst, and sometimes younger cysts within them. Thus, there is a cyst with daughter and granddaughter cysts. Occasionally the daughter cysts develop outside the mother cyst, imperfections in the cuticular layer or accidents to the cuticular layer permitting the escape through it of some of the parenchymatous layer.

3. *Echinococcus multilocularis.*—This form consists of a considerable number of independent cysts surrounded by rather dense connective tissue. The cysts encountered are usually dead parasites.

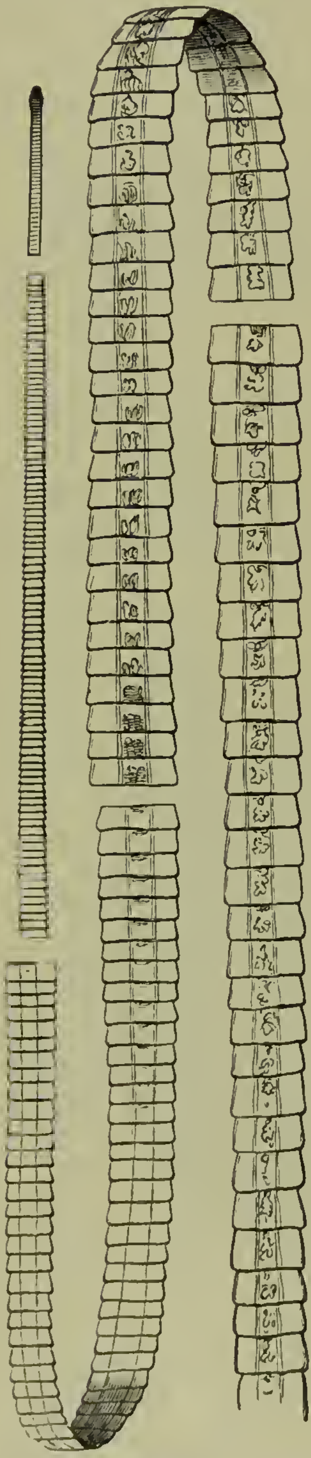

FIG. 168.—Bothriocephalus latus (Eichhorst).

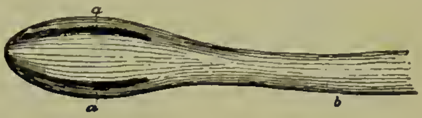

FIG. 169.—Head of Bothriocephalus latus: *a*, *a*, Bothridies; *b*, neck (Blanchard).

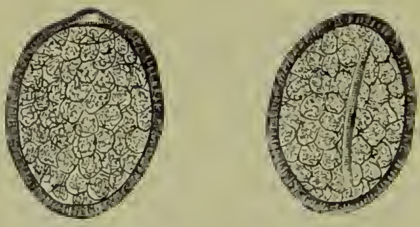

FIG. 170.—Eggs of Bothriocephalus latus (Mosler and Peiper).

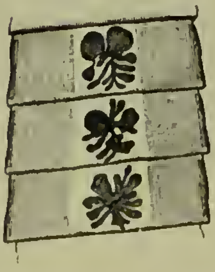

FIG. 171.—Ripe segments of Bothriocephalus latus (Mosler and Peiper).

The echinococcus cyst as it occurs in man may be dangerous or harmless according to circumstances. Its occurrence in parts of the body readily disturbed because of the pressure may be discomforting or dangerous. Rupture of the cysts also has serious results in some cases.

In most cases, however, the parasite is considerably more interesting than dangerous, and when discovered at autopsy, is frequently long since dead. Death of the parasite is succeeded by clouding, inspissation, and mineralization of the contents.

The prophylaxis of echinococcus disease is involved in the proper regulation of the association between man and his friend, the dog. The disease is most frequent in countries and communities in which man lives in too friendly association with dogs.

Bothriocephalus latus.—This is the largest tape-worm, and indeed the largest and most formidable parasite of man. It measures from 5 to 9 meters, and may have as many as 4000 proglottides, which are characterized by great breadth and a very prominent central uterus, which appears as a dark, roset-shaped spot in the center of the segment. The head is elongate and clavate, has no rostellum and no hooklets, but upon each side has an elongate, deep groove. The neck is stouter than in most tape-worms, and the segmentation begins close to the head. The genital opening of each segment is in the center of the posterior edge in the median line. The reproductive apparatus is quite different from that of the other worms, the uterus being coiled instead of complexly branched, as in Tænia solium.

It is supposed that the scolex lives in the pike. The strobile only is known in man. It is supposed that the eggs undergo some development in water before being taken up by the fish and beginning their development in it. It has been experimentally shown, however, that when the embryos of this worm are eaten by man, they develop at once into strobila.

The eggs differ from those of other tape-worms, and the presence of the adult worm in the host can be recognized by an examination of the feces and discovery of the eggs, which are characterized by a kind of hinged lid at one pole.

The worm is more common in Europe, where the pike is more highly esteemed for food than in the United States. It is usually solitary, but many have been found in the same patient. In some cases the worm produces anemia. The entrance of the embryos into man can be prevented by sufficiently cooking the fish before eating it.

B. NEMATODES OR ROUND WORMS.—These are characterized by an elongate cylindric form. They are not divided into segments like the tape-worms, and usually are bisexual instead of hermaphroditic. They are provided with alimentary organs. The females are usually larger than the males. The ova are formed in immense numbers and develop into embryos which more or less closely resemble the adult. The life-history is usually completed within a single host, though intermediate hosts are required for the trichina. In some forms the embryos undergo a certain development outside of the body before entering it. Infection is almost always through the alimentary apparatus, though in the case of the filaria it depends upon the bite of a mosquito.

Ascaris lumbricoides.—This, the common round worm of the intestine, is probably the most frequent parasite of man. The females attain a length of 40 cm., the males, 25 cm. They vary from 2 to 5 mm. in thickness. The color is pinkish white, and the worms closely resemble the common earth-worm in appearance. Upon close examination, however, one finds that the worms are characterized by four longitudinal ridges running their entire length, and that the head is provided with three fleshy hemispheric lips surrounding the mouth. There is an alimentary canal reaching the length of the organism. The sexual organs occupy the posterior half of the body, the sexual opening being at the junction of its anterior and middle thirds. The eggs measure from 0.05 to 0.06 mm. in length and are of an oval form, their surface being protected by a clear, irregular coating. The contents are usually granular, though the embryo worm may sometimes be seen.

The worms inhabit the small intestine. They may be solitary or occur in large numbers. As a rule, they are harmless parasites, although when, from disease, the intestine becomes thinned, they sometimes excite perforation. Their chief pathologic importance is associated with occasional migrations into the upper alimentary passages, the larynx, pharynx, Eustachian tubes, bile-ducts, etc. All these migrations are attended with symptoms varying according to the obstructive or other damage that may be done.

The ascarides of the lower animals are of different species, *Ascaris mystax* being common in cats and dogs, *Ascaris megalocephalus* in horses. It is quite probable that the ascarides of hogs and sheep are identical with those of men, and care should be exercised that, through carelessness about slaughter-houses, the infection does not spread. Each worm passed by a human being should be destroyed by fire, or in some way that will destroy all the eggs. A person infected should be given a strong vermifuge, so that the worms be discharged from the bowels and destroyed. General cleanliness, washing the hands before eating so that all traces of earth be removed, etc., will do much to prevent infection.

Oxyuris vermicularis.—This is the "pin-worm" or "seat-worm" so common among children, though in rare instances also affecting adults. The female worm measures from 10 to 12 mm., the male, from 2.5 to 5 mm., in length. The posterior end of the male is blunt and curved upon itself; that of the female, elongate. The eggs are about 5 μ in length. The embryo worm is often visible within the egg. The parasites live in the large intestine,

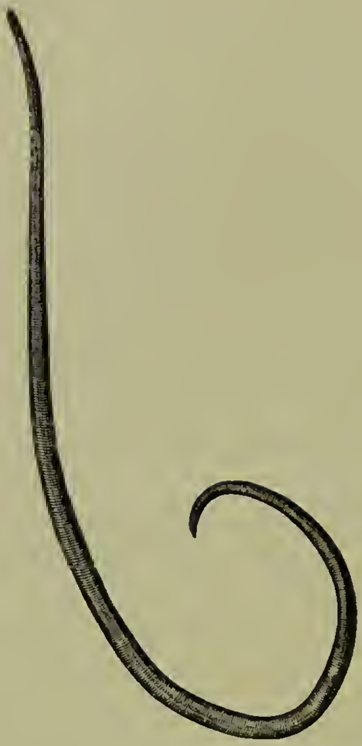

FIG. 172.—Ascaris lumbricoides (female) (Mosler and Peiper).

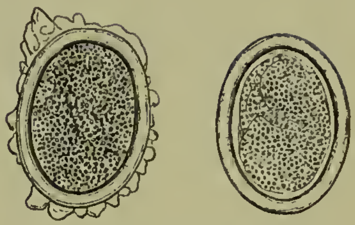

FIG. 173.—Eggs of Ascaris lumbricoides (Mosler and Peiper).

from which they and their eggs are discharged. They usually occur in large numbers. The parasites are harmless, but a tendency to nocturnal migration leads to much annoyance.

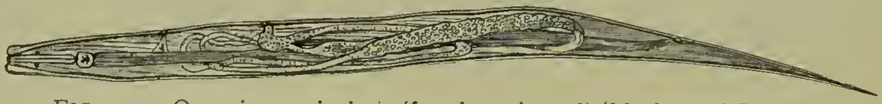

FIG. 174.—Oxyuris vermicularis (female, enlarged) (Mosler and Peiper).

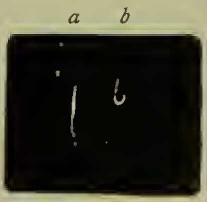

FIG. 175.—Oxyuris vermicularis (natural size): *a*, Female; *b*, male (Mosler and Peiper).

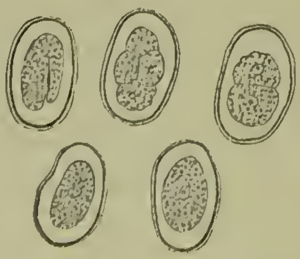

FIG. 176.—Oxyuris vermicularis. Eggs in various stages of development (Mosler and Peiper).

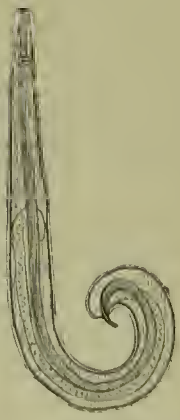

FIG. 177.—Oxyuris vermicularis (male, enlarged) (Mosler and Peiper).

The worms leave the rectum and enter the vagina and urethra in girls, and sometimes pass beneath the prepuce in boys, causing irritation and itching. Masturbation may follow this irritation in boys. Children of both sexes scratch the anus, thus taking up the eggs under and about the finger-nails and subsequently carrying them to the mouth. The eggs being swallowed, hatch in the upper intestine, and the female worms there become impregnated. In this manner the children constantly reinfect themselves, so that the worms usually occur in large, not small, numbers.

The destruction and removal of the parasites already present in the intestine and scrupulous care concerning cleanliness are the best prophylactic measures.

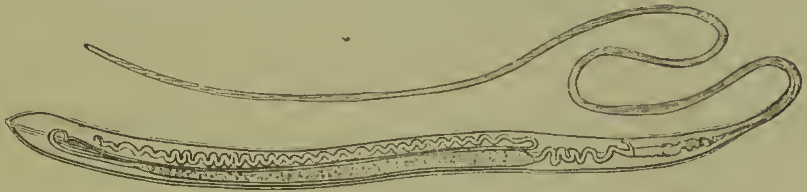

FIG. 178.—Trichocephalus dispar (female) (Mosler and Peiper).

Trichocephalus dispar.—The "whip-worm" is a small and inoffensive parasite of the large intestine of man. It is common in Syria and Egypt. Its peculiarity is that the anterior two-thirds of the body are extremely slender and thread-like, while the posterior third is thicker, like the handle of a flexible whip. In the male the posterior portion is not only thick, but spirally coiled, while in the female it is straighter. The total length of the worm is between 4 and 5 cm. The eggs, which have a peculiar button-like protuberance at each end, resemble diminutive lemons, and are about 0.55 mm. in length.

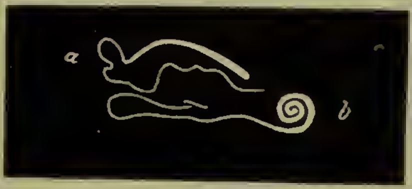

FIG. 179.—Trichocephalus dispar: *a*, Female; *b*, male (natural size) (Heller).

The worms are usually multiple, and live in the cecum and vermiform appendix. The worm is probably harmless, though it has been claimed that it sucks blood and so endangers its host.

Trichina (*Trichinella*) *spiralis.*—This is a small, but troublesome, parasite, which undergoes development in two hosts. It occurs in man, hogs, rats, mice, cats, and other animals. Man becomes infected through eating imperfectly cooked meat, especially pork, containing the embryos in an encysted form.

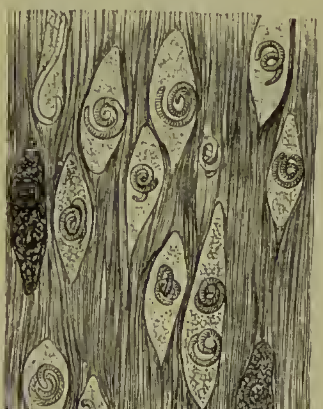

FIG. 180.—Fresh muscle trichinæ (Mosler and Peiper).

The gastric juice dissolves away the wall of the cyst and liberates the embryo, which rapidly develops into a sexually perfect adult, becomes impregnated, and proceeds to discharge embryos. Sometimes these are liberated directly into the intestine; sometimes the female worm burrows beneath the epithelium, connects itself with one of the lymphatics of the intestine, and discharges the embryos there. They are taken through the lymphatics for some distance, and must eventually reach the blood, as the metastatic distribution of the worm is very wide. Most of the embryos finally come to rest in the voluntary muscles, where they coil up and become encysted. The muscles most frequently infected are the diaphragm, the thoracic and abdominal muscles, and lastly those of the limbs. Becoming thus encysted, the worms await the coming of some new animal to devour the muscle in which they lie, in order that further development may go on.

The period during which the worm develops in the intestine is three days. The embryos probably reach the muscles about ten days after. The muscular invasion seems to take place in successive crops. In two or three weeks they become encysted. Some of the encysted worms die and become calcified. The capsules may become mineralized while the worm still remains alive.

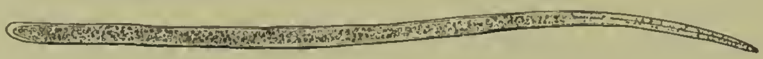

FIG. 181.—Intestinal trichina (female, enlarged) (Mosler and Peiper).

The symptoms are serious. While the embryos are being discharged in the intestine, the host suffers from colicky pains of the abdomen, vomiting and diarrhea, and may go into collapse. As the worms migrate and establish themselves in the muscles the symptoms change to muscular disturbance, with pain and fever. As the worms in large numbers occasion some degeneration and atrophy of the tissues, muscular weakness may be a later symptom.

The adult female worm measures from 2 to 4 mm., the male, 1.5 mm., in length. The eggs develop into embryos while still within the mother. The embryos found in the intestinal tract are from 0.1 to 0.16 mm. in length, the anterior part being thicker than the posterior. Many of them are discharged in the feces and others die.

The remedies against the disease are simple. First, meat should be carefully inspected, and "measly pork" condemned as unfit for food; second, all pork should be thoroughly cooked before it is eaten.

Uncinaria (*Ankylostoma*) *duodenalis*.—This is a small, though dangerous, parasite that lives in the upper intestine of man by sucking blood from the mucous membrane. The female worm measures from 7 to 16 mm., averaging about 11 mm. in length and 0.63 mm. in breadth. The male is shorter and more slender, being from 7 to 11 mm. long and 0.46 mm. in breadth. The head of the worm tapers and is cylindric, and in both sexes is bent at an acute angle. The mouth opening is provided with six sharp, incurved teeth or hooks arranged in three pairs. It opens into an esophagus that occupies the anterior third of the body. The orifice of the excretory pore into which the excretory canal opens is beneath two cervical papillæ, directed posteriorly. A second opening, in the female, is the genital pore that lies below the middle of the abdomen. The posterior end of the female is rounded and tapering. The tail of the male, however, enlarges, is truncated, and shows a peculiar three-fold cuticular process—the copulatory bursa—looking a little like an open umbrella. From it two chitinous spines project.

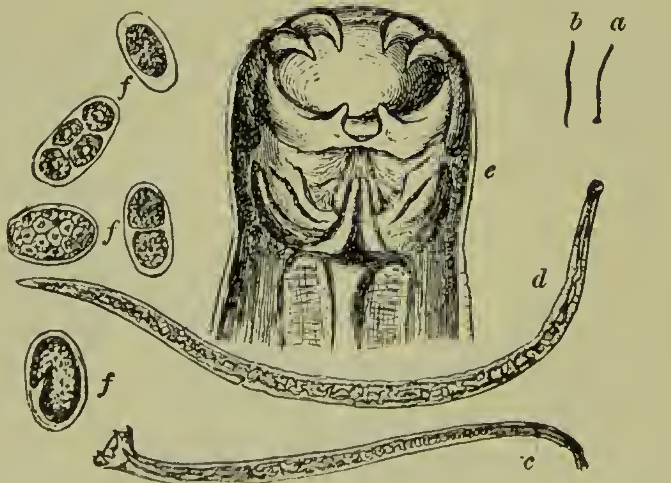

FIG. 182.—Uncinaria duodenale: *a*, Male, natural size; *b*, female, natural size; *c*, male, magnified; *d*, female, magnified; *e*, head, greatly magnified; *f*, *f*, *f*, eggs (von Jaksch).

The harm done by the worm results from its frequent bites, which bleed subsequently, the loss of blood when many parasites are present and moving from place to place and frequently biting the mucous membrane, being very considerable, and even in some cases ending in symptoms not easily differentiated from pernicious anemia. A characteristic of the anemia is a marked *eosinophilia*.

The eggs of the parasite, which appear in the feces of infected persons, are oval, thin shelled, doubly contoured, and measure from 0.36 to 0.63 mm., according to different observers. The eggs are fertilized in the organs of the female. In the human intestine they segment twice, but further development has not been observed. The number of eggs is immense, Leichtenstern having estimated that one stool contained 4,216,930 eggs of this parasite. The eggs develop when the stool is exposed to oxygen, and in from three to four days the embryos are visible in the eggs; in about two days more they break out and begin active movements. At this time they measure from 0.2 to 0.5 mm. in length and from 0.015 to 0.017 mm. in breadth. They begin to grow at once, and soon produce an additional encapsulating cuticle in the form of a thick hyaline sheath. In some cases the sheaths mineralize. The capsule thoroughly protects the embryo from drying. Water seems to be the natural habitat of the larva. Infection has been thought to take place through drinking infected water, and, indeed, experiment has shown that when the larvæ just described are taken into the human intestine, they develop into adult worms.

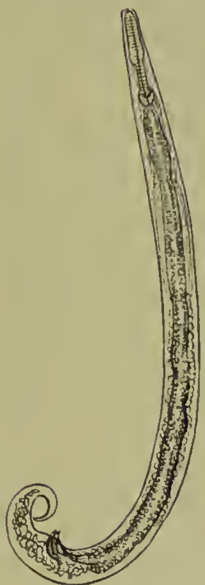

FIG. 183.—Anguillula intestinalis (female) (Perroneito).

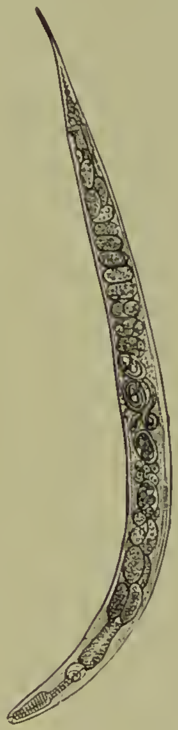

FIG. 184.—Anguillula intestinalis (male) (Perroneito).

This is, however, probably not the only method of infection, as Looss has shown experimentally that when water containing the embryos is brought into contact with the human skin, the embryos begin to burrow through by way of the hair-follicles and sweat-glands, a form of "ground itch" depending upon the penetration of the skin of the feet and legs by these embryos.

The adult worm lives in the small intestine and may be present in small or large numbers. It usually attaches itself firmly to the mucous membrane, where its head appears in contact with a petechial point about which there is a considerable sized pale area. When the worm detaches and moves to another point, the seat of its attachment continues to bleed for a considerable time, so that when the worms are numerous, they may be the cause of a marked anemia, which may become so intense as to resemble pernicious anemia.

A curious thing about the worm is that it seems for some reason to infect persons whose labor is in tunnels, mines, and other earthworks, very severe infection having been observed among the workmen who dug the St. Gothard tunnel.

The prophylaxis would seem to be simple. The stools containing the eggs should all be carefully destroyed. Water likely to contain the embryos should be carefully boiled. Fingers soiled with earth should not be carried to the mouth or used to handle food. Care should be exercised to prevent water containing the embryos from coming in contact with the skin so that workmen in infected districts should wear rubber boots, etc.

Uncinaria americana.—This is a slightly smaller, closely related worm of wide distribution in America. It has a much smaller head, smaller and blunter teeth, and is probably much less dangerous as a parasite than its European relative.

Anguillula intestinalis.—This is an actively motile little worm, measuring about 2 mm. in length, inhabiting the intestine and the ducts communicating with it. The female lives only in the intestine and discharges parthenogenetic eggs from which both male and female embryos develop. These embryos differ so in appearance from the adult that for a long time they were supposed to be a different worm and were called *Anguillula stercoralis.* They are not found in fresh feces, and at autopsy only after the cadaver has been dead for some time. The female worm is the larger, and has its posterior extremity drawn out to a fine point and straight. The male has a thicker and more curved posterior extremity and shows two spicules on the cloaca.

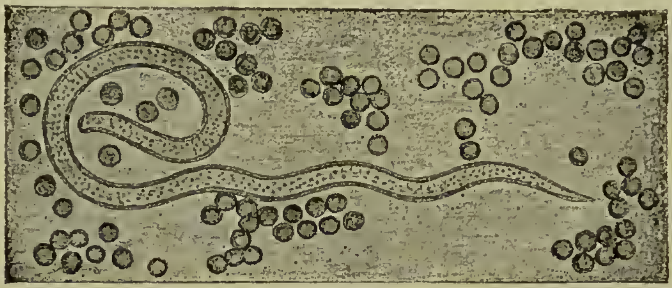

FIG. 185.—Filaria embryo, alive in the blood (F. P. Henry).

The embryos grow into females of the form called Anguillula stercoralis, and by this indirect stage subsequently into Anguillula intestinalis.

The worm occurs chiefly in Asia and especially in Cochin-China. It is of no pathologic importance.

Filaria sanguinis hominis.—This name was originally applied to a small worm that Wucherer found in the urine of a case of hematuria, which was later found in the blood, in the lymphatics, and in chylous urine. It seems that the worms found under these different conditions are not all the same, hence the original name has become common to what are now recognized as a number of different species.

The most common species is that known as *Filaria nocturna.* The adult worm is very rarely found. It measures from 8 to 10 cm. in length, and lives in the larger lymphatic vessels. No eggs are laid, but living embryos are discharged in large numbers into the lymphatics, from which they enter the blood. These embryos are distinctly vermicular, and measure about 0.216 mm. in length and 0.004 mm. in thickness. Each embryo is surrounded by a hyaline sheath. Its structure is homogeneous, except at the center, where it may appear granular.

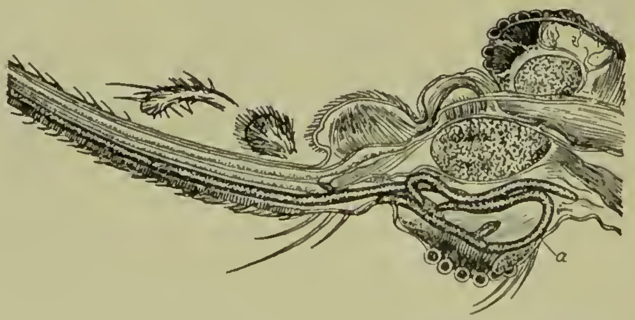

FIG. 186.—Filarial worm (*a*) in proboscis of Culex pipiens.

The embryos being in the blood, escape into the urine with the corpuscles when attacks of hematuria occur, hence the original discovery of the parasite in the urine. Through some not understood peculiarity the embryos appear only in the circulating blood during the hours of rest. For most persons this is at night, but when the conditions of life are altered and one works at night and sleeps by day, the parasites appear in the blood in the daytime.

The parasites may be quite numerous, several embryos being present in a single cover-glass preparation of the blood. They are active in their movements, wriggling actively, but not appearing to progress.

Manson was the first to suggest that the mosquito might be concerned in the further life-history of the filaria, and by feeding mosquitos upon blood containing them, observed that the embryos underwent a further growth in the insects. He supposed that, having withdrawn the insects in the blood they sucked, they flew off to pools of water in which to deposit their eggs, and, dying there, the filaria contained in their bodies were set free, continued their development in water, and infected man by water which he drank or by boring through his skin as he bathed.

Low, however, observed that the filarial embryos after entering the mosquito's body cast their sheaths, bore through the intestine of the insect, enter the body cavity, and find their way to its head, where their tendency is to enter the proboscis. This led him to believe that the infection of man takes place through mosquito bites, the warmth and taste of blood which they receive when the insect bites causing them to leave their position in the proboscis and enter the wound.

In many cases the filaria live in the body without occasioning any symptoms. In other cases they cause pains in the back, abdomen, perineum, etc., chiefly from lymphatic obstruction, and lead to various enlargements, such as lymph-scrotum and elephantiasis. The worms have sometimes been found in the lymph. The lymphatic obstructions may lead to chyluria, and the presence of worms in the blood may cause hematuria.

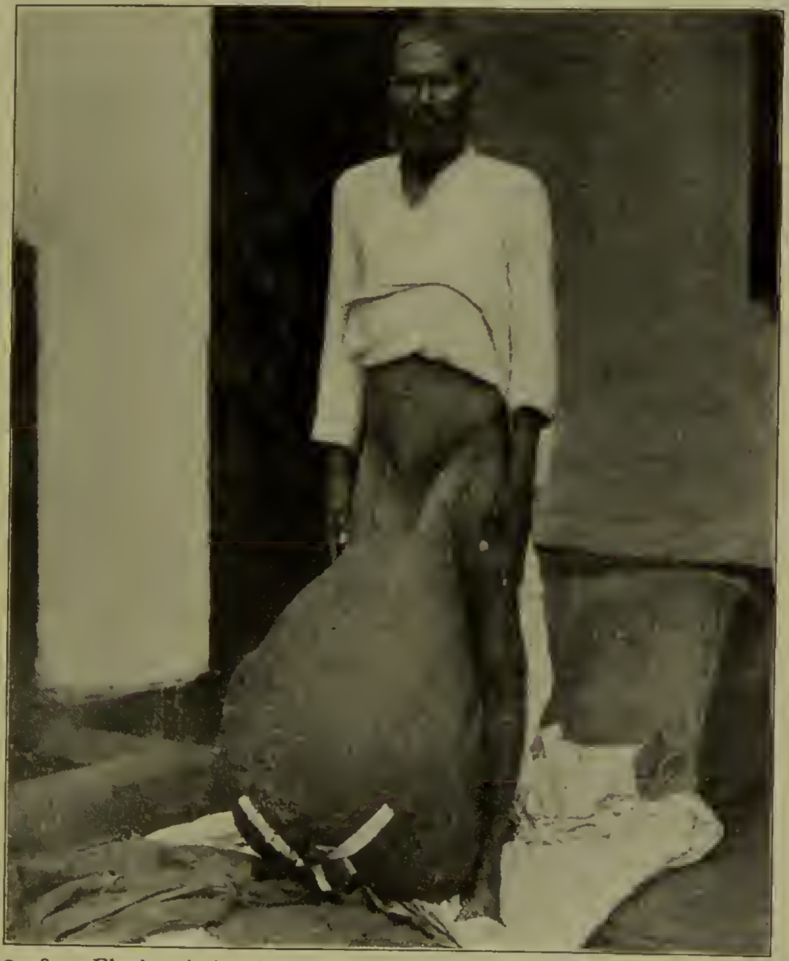

FIG. 187.—Elephantiasis of the scrotum. Weight, 110 pounds. Successfully removed (Cantlie).

The *Filaria perstans* occurs in the blood at any time, night or day. Manson believed it to be the cause of the *African sleeping sickness*, as well as of a certain skin disease known as *craw-craw*. Only the embryo worms are known. The *Filaria diurna* occurs in the blood only in the daytime. Other forms of filaria have been found in the lens of the eye (*Filaria lentis*) in a case of cataract; in a pustule on the lip (*Filaria labialis*); in the mouth of a child (*Filaria hominis oris*); and in the urine (*Filaria restiformis*). Filaria also occur in the dog and in other animals.

The Culex ciliaris or Culex pipiens is the definitive host. The prophylaxis is simple, as the free use of wire netting in the windows and nets over the beds seem to be as much as can be done at present in preventing infection.

Filaria medinensis.—The "Guinea-worm" is a round worm about a meter in length and very slender. It occurs in the tropical districts of Asia and Africa, especially in Arabia, Abyssinia, and Guinea. Only the adult worm is known, and only the female is known with certainty. It inhabits the subcutaneous tissue of the lower extremities, where it occasions inflammatory lesions not unlike carbuncles. How the infection originally takes place is not known, but it is thought that the embryos are able directly to penetrate the skin from water in which they are present. Another view is that the embryos live in minute water crustaceans (cyclops), and that infection takes place by swallowing these and is always gastro-intestinal. The greater part of the body of the worm consists of uterus, and from an ulcer from which the tip of the worm sometimes protrudes enormous numbers of embryos are discharged, this discharge taking place particularly when water is brought in contact with the ulcer, so that it is inferred that the embryos live in the water.

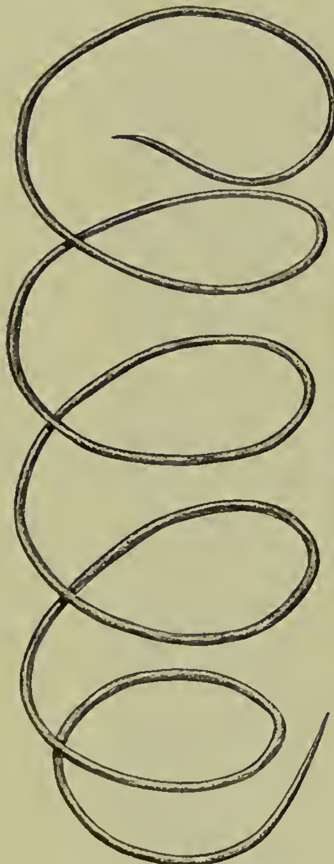

FIG. 188.—Filaria medinensis (anatomic collection, Greifswald).

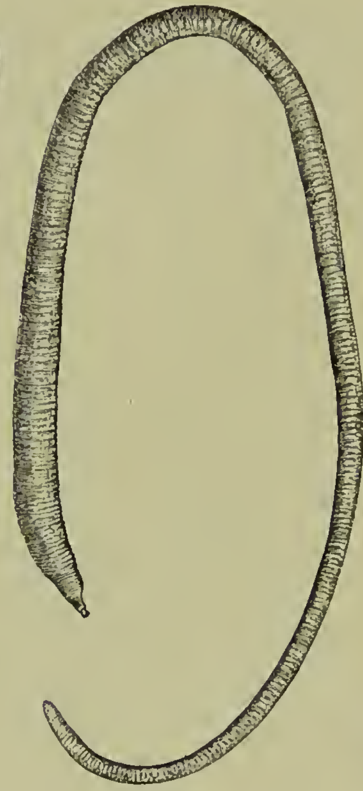

FIG. 189.—Echinorrhynchus gigas (female) (Mosler and Peiper).

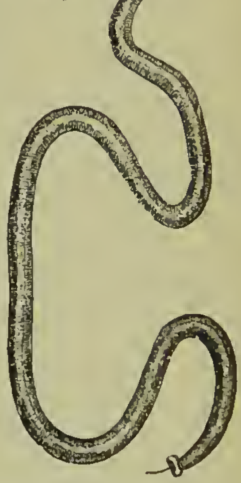

FIG. 190.—Male of Eustrongylus gigas (natural size) (Leuckart).

Echinorrhynchus gigas.—This is a large round worm living in the small intestine of the hog, and occasionally infecting man. The female measures from 31 to 50 cm.; the male, from 7 to 10 cm., in length. The head is armed with a retractile proboscis-like rostellum armed with six rows of hooklets, each row having eight spicules. The intermediate host is thought to be the larva of a beetle.

Eustrongylus gigas.—This is also a large round worm, about 1 meter in length, which is sometimes found in the pelvis of the kidney, ureter, and bladder of horses, cattle, and dogs, and very rarely in man. The male is about one-third as large as the female. It is of a brownish or blood-red color. The anterior end is retracted, the mouth surrounded by six papillæ. The posterior end is expanded, and a spicule projects from the cloaca.

Strongylus longevaginatus.—This is a rare round worm occasionally found in the lungs of sheep, swine, and rabbits. It has also been found in children. The female measures 26 mm., the male 15 to 17 mm., in length and from 0.55 to 0.7 mm. thick. The color is yellowish white. The uterus is filled with eggs containing coiled embryos. The developmental stages of the parasite are unknown.

C. TREMATODE WORMS.—These comprehend a peculiar and somewhat varied group, consisting chiefly of flattened elliptic organisms that attach themselves to certain structures from which they derive their nourishment by sucking. The individuals are usually hermaphroditic, but in some, two sexes occur. The developmental cycle may be simple or complex, and usually requires the sojourn of the embryo parasite in an intermediate host.

Distoma hepaticum.—This worm, known as the "*liver fluke*," inhabits the bile-ducts of sheep and occasionally of man, sometimes occurring in large numbers and provoking dangerous symptoms by obstruction of the biliary passages and enlargement of the liver, with later degeneration and cyst formation. The worm is flattened and elliptic, and pointed bluntly at each end. It measures from 15 to 35 mm. in length, and from 6 to 20 mm. in breadth. The head is small, and forms a kind of snout with a sucker at the end. A second sucker arises from the ventral surface immediately behind the short neck. Between these two suckers the sexual opening is situated. The uterus, which makes up the chief part of the body, is elongate and consists of a central tube with numerous lateral dendritic branches. The testicular organ consists of a delicate series of coils. The animal is hence hermaphroditic. The eggs are oval and measure 0.09 mm. by 0.14 to 0.15 mm. The one end is slightly flattened. The eggs develop into embryo worms in water. These are ciliated on all sides. Leuckart believes that a water-snail (*Limnæus minutus*) is the intermediate host. The worm may produce no pathologic changes or may bring about inflammatory and obstructive disease of the bile-ducts.

The choice of an upland dry pasture for sheep and the selection of a pure supply of drinking-water for both animals and men will probably do much to lessen the frequency of the infection.

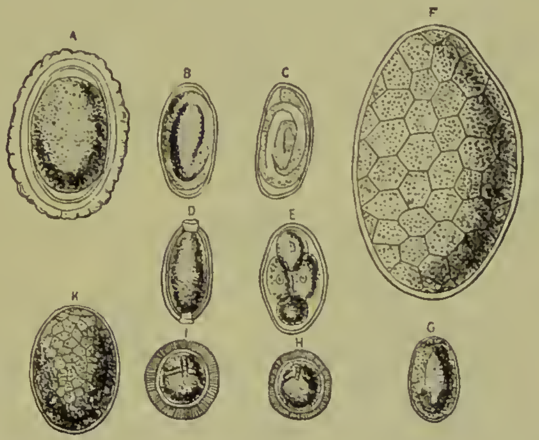

FIG. 191.—Eggs of various worms found in the alimentary canal of man: A, Ascaris lumbricoides; B, C, Oxyuris vermicularis; D, Trichocephalus dispar; E, Uncinaria duodenale; F, Fasciola hepatica; G, Dicrocœlium lanceolatum; H, Tænia solium; I, Tænia saginata; K, Bothriocephalus latus. × 400 (Mitchell).

Distoma lanceolatum.—This is a smaller and more slender distoma, measuring from 8 to 10 mm. in length, and having, in general, a lancet shape. The anterior end of the body is the more pointed. It has two suckers, like the Distoma hepaticum, but they are more widely separated. The snout is provided with a spread-out membrane somewhat like an umbrella. The eggs are oval and measure from 0.04 to 0.045 by 0.03 mm. The embryo seems to develop in the body of the mother, and is pear-shaped and ciliated anteriorly. The intermediate host is unknown.

The parasite occurs under the same conditions as its close ally, and the two species frequently occur together.

No special symptoms referable to this parasite have been described.

Distoma Hæmatobium.—This worm is an extremely common and wide-spread parasite of Africa and other tropical countries, but especially of Egypt, where Bilharz, who discovered it, has calculated that at least one-fourth of the native population is infected. It usually occurs in natives, usually among the lower classes, and chiefly among boys from nine to sixteen years of age.

The worm has both sexes, which live in the portal, abdominal, and cystic veins. The eggs are produced in immense numbers, collect in and break up the capillaries, and cause ulcerations and other small lesions from which the eggs, together with considerable blood, escape into the urine.

The male worm is the stouter and larger of the two. It measures from 12 to 14 mm. in length by 1 mm. in breadth, and is flattened. The surface is rough and covered with irregularities. The flat body of the male usually curves so as to inclose a central canal (canalis gynæcophorus), into which the female worm creeps for fecundation. The female is longer, more slender, and smooth on the surface. It measures from 16 to 18 mm. in length by 0.13 mm. in breadth. The usual suckers appear upon the head. The alimentary canal ends in a bifid cecum between the terminations of which the sexual organs are situated.

The eggs are often contained in large numbers in the uterus and vagina of the female, while those escaping collect in masses blocking the capillaries, and appearing, on section, to the naked eye as small grayish-white points. They measure about 0.12 mm. in length and 0.04 mm. in breadth. Their chief peculiarity is that each is provided with a spine that usually projects at one end, though sometimes from the side. The shell of the egg is thin, the contents granular. The embryos do not escape until long after the eggs are formed, and appear as cylindric bodies with conically pointed posterior ends and elongated snouts anteriorly. They are ciliated and motile.

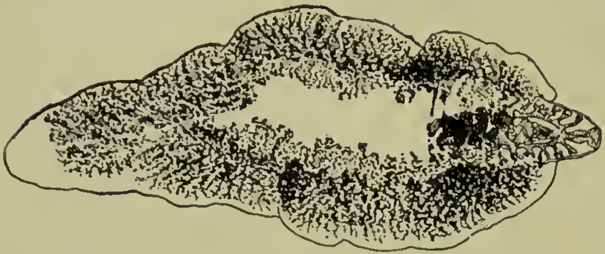

FIG. 192.—The liver fluke, Fasciola hepaticum.

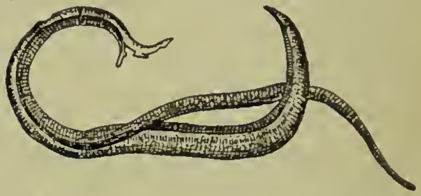

FIG. 193.—Human blood fluke (Schistoma or Distoma hæmatobium). The female is partially within the canalis gynæcophorus of the male. × 5 (Leuckart).

The developmental history of the embryos and the mode of human infection are unknown. It is supposed that they live in water and enter the body by the alimentary tract.

The worms when in the body lie in dilatations of the veins, especially in dilatations of the cystic veins, from which Bilharz repeatedly extracted them at autopsy. The wall of the bladder becomes chronically inflamed and ulcerated in consequence of the pressure of the groups of eggs and parasites near the surface. The urine is first discharged; as the bladder contracts after urination, blood is expressed and hemorrhage occurs.

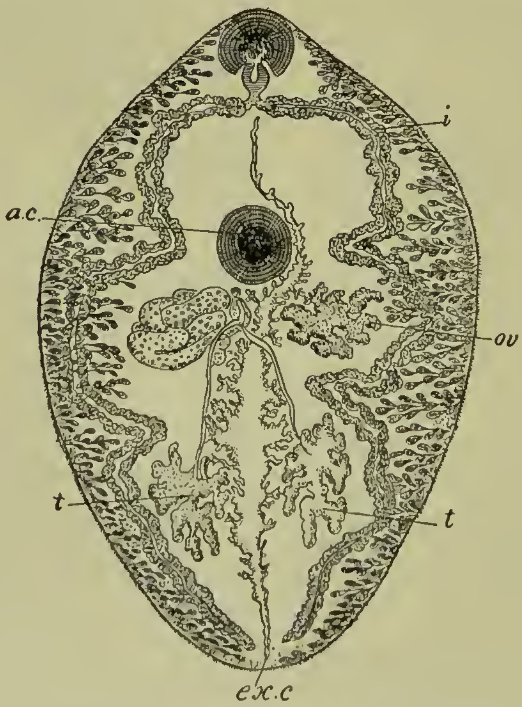

FIG. 194.—Ventral view of a lung fluke from man, showing anatomy: *ac*, Acetabulum; *ex.c*, excretory canal; *i*, intestinal cæca; *ov*, ovary; *t*, *t*, testicles (Leuckart).

If the infection depends upon the embryos in drinking-water, the prophylaxis is easily achieved by careful boiling—a precaution that has so frequently been advised, that in the tropics no water should be consumed without it.

Paragonimus westermanii (*Distoma pulmonale or lung fluke*).—This is a rare parasite in man, but one that has a wide-spread distribution among the lower animals, having been observed in the tiger, cat, dog, and hog. It is more frequent in oriental and tropical countries than elsewhere.

It is a hermaphrodite, somewhat resembling the Distoma hepaticum, but thicker and more rounded in form. It measures from 8 to 20 mm. in length and from 2 to 5 mm. in breadth. The general arrangement of the suckers and genital opening are similar to the liver fluke. Eggs are produced in large numbers and discharged from the lung in the sputum. Under proper conditions they develop into *miracida* or ciliated embryos which seem destined to live in water. The life cycle has not been established, but it seems possible that the intermediate host is a snail—probably a *limneus* called "*nina*." The intermediate host not being known, it is impossible to say how infection takes place. The adult worms live in the bronchi, where they occasion a hemorrhagic hemoptysis.

ARTHROPODA.—The amount of space that would be occupied by any adequate description of the larger arthropods, such as fleas, lice, bedbugs, ticks, and maggots, that occasionally derive their nourishment from the surface and cavities of the human body, would be so considerable that we leave these comparatively familiar parasitic forms without other mention, and describe only a few which, because of their importance or minuteness, are less well known to the average reader.

Sarcoptes scabiei or Acarus scabiei.—The "itch-mite," which was the cause of much dissension among the scientific students of Paris in the early part of the nineteenth century, was finally demonstrated to be the cause of *scabies*, or "the itch," by a Corsican student named Renucci in 1834, the discovery of the male mite being achieved by Kraemer in 1846. The mites are very small, the female, however, being larger than the male, and measuring 0.45 mm. by 0.35 mm. The male measures 0.23 mm. by 0.16 mm. To the naked eye the mite appears simply as a minute yellowish-white point. The general shape resembles that of a tortoise, in that it is elongate and rounded, with wavy transverse folds or ridges. Upon the back there are numerous spines and scale-like elevations and thorny processes. The head, which can readily be recognized, is armed with six bristles. There are four pairs of legs, each composed of five joints. The anterior limbs terminate in suckers attached to long pedicles. The other limbs end in bristles. The female has two vaginæ, one of which is used for copulatory purposes, the other for the extrusion of ova. The eggs are elliptic, have smooth skins, and measure about 0.16 mm. long and 0.11 broad.

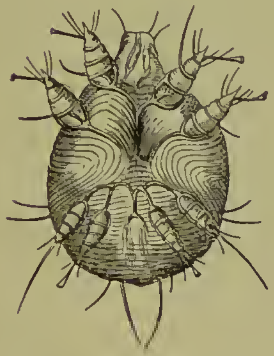

FIG. 195.—Male acarus (after Anderson).

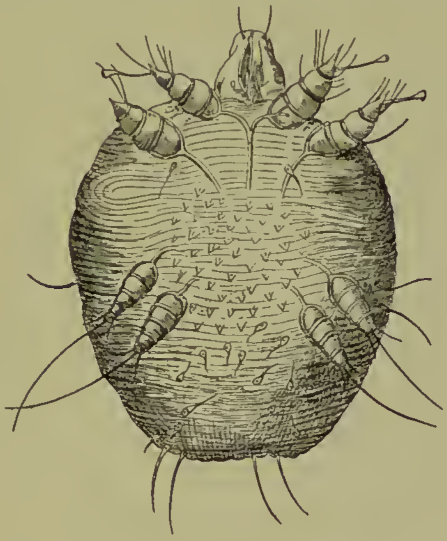

FIG. 196.—Female acarus (after Anderson).

The adult female lives in a burrow that she makes in the superficial layers of the skin. The animal readily bores its way down to the *rete mucosum* when placed upon the skin, and so causes pain and itching. The mite seems to subsist upon the epithelial cells of the lower layers of the skin. The female continues to produce and discharge ova so long as she is sequestered in the burrow, gradually boring her tunnel or burrow deeper and deeper, moving on and on and leaving the embryos behind.

The burrow has, however, numerous small openings that serve to let in air and to let out the embryos. The parasites and their burrows can be seen with the naked eye, but much better with a lens. They occur chiefly upon the hands, but also upon other, especially frequently handled, parts of the body, such as the penis, buttocks, elbows, knees, etc. The burrows appear as delicate white lines, the mite lying as a distinct point in the blind end. They vary from one to several centimeters in length.

The development of the larva in the eggs requires from four to seven days. The embryos differ from the adults in that they are smaller and have only six legs. They soon escape from the burrows, wander about upon the surface of the skin, then make little burrows in which to cast their skins, which they do three or four times, so that it takes about fourteen days for the embryo to attain sexual perfection. The life of an itch-mite is two or three months.

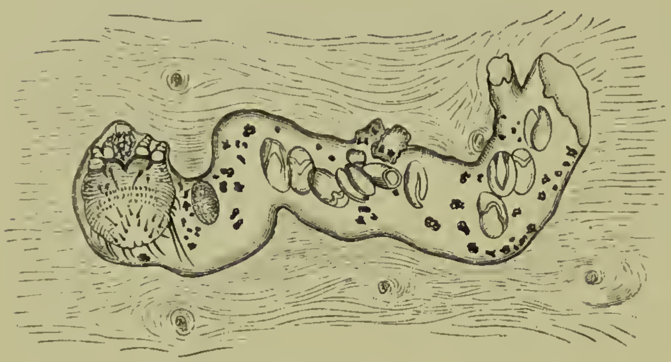

FIG. 197.—Acarus burrow under skin of human finger (Fürstenberg).

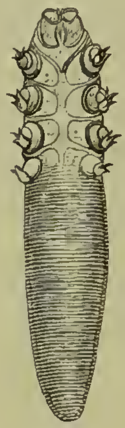

FIG. 198.—Demodex folliculorum (Mosler and Peiper).

Itch-mites are not parasites of man alone, but infect many different animals—horses, cattle, hogs, dogs, cats, rabbits, camels, dromedaries, rats, etc. The parasites of different animals are probably of different species, as they rarely survive longer than one generation when transplanted.

Contagion depends solely upon the accidental adhesion of a sexually ripe female mite to the skin that has been in contact with an infected person.

Demodex Folliculorum.—This is the sebaceous gland mite. It is an innocent parasite of man, but occasionally causes a fatal skin disease in dogs. It occurs in man, dogs, cats, swine, and other animals. The mites measure from 0.3 mm. to 0.4 mm. in length, and from 0.04 mm. to 0.05 mm. in breadth, the female being the larger. It has an elongate, somewhat worm-like appearance, with four pairs of legs on the anterior half of the body. The mites live in the hair-follicles and sebaceous glands and in the comedones, several parasites usually living in the same area. They also occur in acne pustules, but probably accidentally.

CHAPTER IX.

IMMUNITY.

In its broad sense, immunity means exemption from disease. In the sense in which we here employ it *immunity* is resistance to disease; *susceptibility*, the opposite condition, receptivity to disease. *Predisposition*, also called *dyscrasia*, is abnormal susceptibility.

Of all the phenomena of disease, there are few so complicated as those that have to do with the ability of the organism to defend itself against injurious agents.

The condition may be *natural*, by which is meant an inherited immunity peculiar to animals of one kind, or *acquired* through various accidental conditions occurring during the life of an individual and peculiar to it, not its kind.

Immunity is nearly always *relative*, as is well illustrated by the case of the hedgehog, which can resist the effects of serpents' venom in amounts ordinarily injected by the snakes, but will succumb to larger doses; absolute immunity is seen in the cases of certain of the lower animals which feed habitually upon poisonous plants and roots.

Immunity is also divided into *histogenic* and *hematogenic* forms. The former depends upon tolerance of the cells to the noxious influence, or their ability to combat it; the latter upon substances contained in the blood, as alexins and antitoxins, which annul the toxic substances.

Active immunity is histogenic or cytogenic in origin, depending upon the activity of the cells in protecting themselves.

Passive immunity is hematogenic and depends upon the presence of vicariously prepared substances.

I. *Natural immunity* is active and histogenic. It is sometimes accompanied by an active phagocytosis, as in the case of frogs injected with anthrax, in which the bacteria soon become incorporated by the leukocytes. In many cases, however, there is no positive evidence that phagocytosis plays any important rôle in the phenomenon which seems to depend upon the destruction of the micro-organisms by bactericidal substances in the body juices.

II. *Acquired immunity* may depend upon a variety of conditions by which the individual is modified so as to become resistant against certain injurious agencies. The relativity of immunity has already been discussed, but must be considered again in this connection, for acquired immunity consists in large measure of the exaltation of a normally existing but feeble resisting power. Thus, when an animal is injected with one of the proteid poisons,—venom, tetanus toxin, ricin, etc.,—the dose being just short of that which would otherwise be fatal, it becomes ill with the specific symptoms, but recovers. In the reaction the animal is changed in some way, for it will not again react in the same manner, and to the same degree, to the same dose. It has acquired a certain degree of immunity or tolerance, the origin of which is, in the present state of knowledge, very uncertain.

If an animal be inoculated with attenuated black-leg virus, it is made ill, and an infectious process is set up which may cause definite symptoms.

After recovery the animal will resist inoculation, experimentally or naturally, with germs of the highest virulence without becoming very ill. After one or two injections of attenuated anthrax cultures highly susceptible animals become able to resist virulent bacilli. After vaccination men resist smallpox. Not only do experimental evidences thus accumulate to interest us, but clinical evidences of body changes produced by disease abound. It is said that a second attack of yellow fever in the same person is unknown. Scarlatina, measles, mumps, rötheln, etc., of the childhood's diseases rarely occur more than once or recur only at long intervals. It is clear that because the germs of these diseases have lived in the body it has become changed, strengthened, and is able to combat them thereafter.

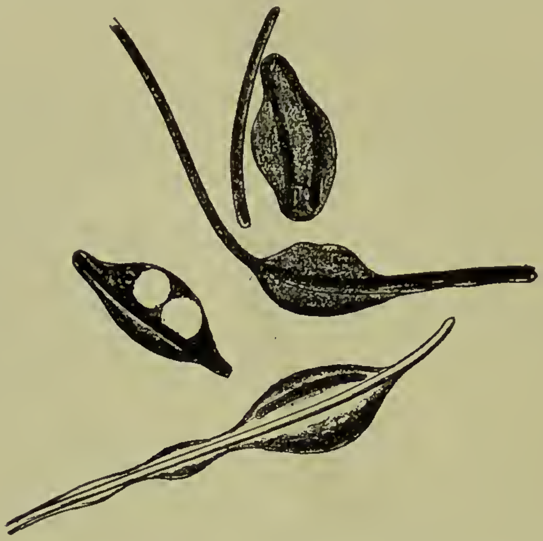

FIG. 199.—Phagocytic cells with incorporated bacilli (Metschnikoff).

It is not impossible that the natural irritability of the tissues has something to do with the acquired resistance attained by contact with bacteria. Nearly all acquired immunity is histogenic, and depends either upon the direct activity of the cells, as shown by phagocytosis, or upon the production of alexins, by which the bacteria of their toxins are destroyed. It may be possible that the first occurrence of a specific disease is accompanied by a certain stimulation of the cells, whose irritability to the hitherto unknown stimuli causes them to contract and become inactive. If once they are able to endure without injury the effects of the irritation, the same stimulation will not again influence them to the same degree, and a definite grade of immunity is attained. Thus, in cases of black-leg vaccination, it has been

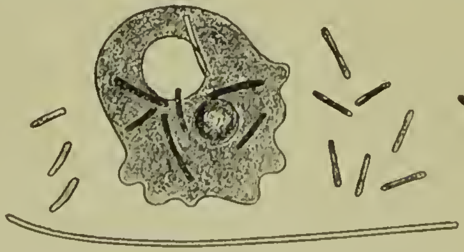

FIG. 200.—Leukocyte with incorporated bacilli, illustrating phagocytosis (Metschnikoff).

found that in the first attack the phagocytes often refuse to take up the bacteria, so that for a time there is a varying degree of extension and limitation of the disease process. By and by the phagocytosis becomes more active, the bacteria are taken up and destroyed, and the animal recovers. In all subsequent infections the leukocytes immediately take up the bacilli and destroy them.

Acquired immunity depends in part upon antitoxins. Experiments made to show that it is the antitoxin formed in the infectious processes that confers the immunity usually fail to demonstrate the presence of sufficient antitoxin in the blood, and all the evidence points to the gradual elimination of the antitoxin by the excretory organs, so that it is almost certain that permanent acquired immunity cannot depend upon it.

The artificial introduction of antitoxic serums into animals invariably brings about perfect immunity against the disease for which the antitoxin is specific, but induces immunity of purely passive and hematogenous character of limited duration, and persisting only so long as the antitoxin remains in the blood.

Spontaneously acquired immunity is illustrated in yellow fever, which is acquired by accident, but which, upon recovery, leaves a permanent immunity behind it. It may also result from accidental infection with a slightly different disease or a modified form of the same disease, as in vaccinia, which, when accidentally acquired from the cow's udders during milking, conveys immunity against small-pox.

Experimental immunity may be the result of intentional infection with the cause of the disease, as in the old-fashioned inoculation against small-pox, or by inoculation with *vaccines,* such as are now used to prevent anthrax and black-leg, and consist of attenuated bacteria specific for the disease. It may also result from a treatment described as "*immunization,*" in which carefully regulated, frequently repeated, progressively increasing doses of the bacterial or other poison are given until tolerance is acquired and immunity attained. This form of immunity is one of the most difficult to understand and merits extended discussion under the term forced immunity.

Forced immunity is an unnatural process by which the resisting powers may be increased to an extreme degree. It is most interesting and instructive to observe that though it is possible to render naturally susceptible animals immune against certain poisons and infectious micro-organisms, in amounts many times that which must have been fatal in the natural state, this increase of resistance cannot go on indefinitely. This fact is well shown in the experimental work done in connection with tetanus and diphtheria in the production of the antitoxins. The horses or other animals used are given frequently repeated, constantly increasing doses of the respective toxins during a period of time extending over months, and finally acquire an extraordinary tolerance, by which they can endure hundreds of times the originally fatal dose of poison. It appears as if the endurance was indefinite, yet if the dosage is continued beyond a certain point, which probably differs with each individual, the tolerance ceases, signs of poisoning immediately appear, and the animal may finally succumb to doses much smaller than those it has been in the habit of receiving. This phenomenon is not at all to be confounded with the "cumulative action" of drugs, for if one is careful not to overstep the mark of tolerance, the administration of properly regulated doses may be persisted in almost indefinitely.

The most interesting phenomenon of forced immunity is the appearance in the blood of a new protective body known as *antitoxin. By antitoxin is meant a peculiar protective energy manifested by certain proteids contained in* *the blood-serum of animals with forced immunity.* The protective nature of the antitoxin is observed when blood withdrawn from the animal is introduced into another animal, which immediately develops a degree of immunity exactly in proportion to the quantity and strength of the blood injected. The subject has been most thoroughly worked over in relation to diphtheria and tetanus, serpent's venom, and ricin and abrin, and for all of these there are specific antitoxins which are now produced commercially and investigated most accurately as to the exact protective strength contained, this strength being expressed in units, arbitrary in nature and varying in exact significance with each kind of serum.

Antitoxicity is a phenomenon of immunity. The tolerance attained by the animal during forced immunization does not depend upon the antitoxin, else the phenomenon of hypersensitivity to the poison mentioned above could not occur, and the tolerance to the poison would be unlimited.

The action of antitoxin is not exerted upon the bacteria. It is, as its name suggests, an antidote for the toxin. Antitoxins are formed by immunization against ricin, abrin, venom, arsenic, and other poisons not bacterial in origin, as well as the powerful micro-organismal poisons. The protective power of the antitoxins, therefore, depends upon action upon the poisonous products of the bacteria, not upon the destruction of the bacteria themselves.

In what manner the antitoxin annuls the effects of the poison is very uncertain. It is thought to be by a direct chemical action, and much evidence has been brought forward to show this to be the case. Thus, when a certainly determined fatal dose of toxin is mixed with a carefully proportioned dose of antitoxin that will annul its effect, not only can this mixture be introduced without harm into an animal, but ten times and one hundred times this fatal dose plus ten or one hundred times the protective dose can likewise be given without harm. It has been shown that when ricin and antiricin are brought in contact with each other, a definite chemical reaction takes place. If animals immunized by antitoxin injections, so that subcutaneous injections of the tetanus toxin are without effect, are injected with the toxin into the brain, they succumb. Behring has, however, explained this in such a manner as to make it support the theory of chemical neutralization, for he observes that the antitoxin in the blood-vessels of the animal escapes slowly through the endothelial cells of the capillaries, not being a dialyzable substance. If, however, the toxin is injected into the brain, where it can act upon the nerve-cells before it comes in contact with the antitoxin, its effect is apparent. If, however, during the operation of injecting into the brain, the blood-vessels are damaged so that the blood may flow out and mix with the toxin, the antitoxin it contains acts upon the toxin, neutralizes it, and no effect is noted.

Others reject the chemical theory and view the activity of antitoxin as the result of tissue stimulation. In disproof of the chemical theory it has been shown that if mixtures of venom and antivenene were made, so as to be neutral for rabbits, and were then heated to a temperature destructive to the antivenene, but not destructive to the venom, the protective power disappeared, leaving the venom unchanged and capable of killing rabbits; that mixtures of toxin and antitoxin of tetanus which were harmless for animals of one species, were still poisonous for those of other species, showing that uncombined toxin remained and that mixtures of toxin and antitoxin neutral for healthy animals were poisonous for weak or ill animals of the same species.

An important point in connection with antitoxins is the specificity of their action. Antitoxins are, as a rule, specific for those particular toxins by whose stimulations they were produced. There are, however, enough exceptions to this to make it probable that the antitoxin is specific only in that it excites to activity those particular cells of the body that are especially acted upon by the related toxin. Thus, tetanus antitoxin protects perfectly against tetanus, and partially against serpent's venom, but is entirely devoid of protective action against diphtheria, ricin, abrin, etc. Antivenene protects perfectly against venom and partially against abrin, but is inactive against diphtheria, tetanus, and ricin. Antiabrin protects perfectly against abrin, and incidentally exerts some protection against diphtheria toxin, serpent's venom, and ricin. Diphtheria antitoxin protects only against diphtheria.

Antitoxins are but one class of anti-bodies formed by the stimulated organism, and since their discovery there have been demonstrated many others whose actions antagonize rennet, dissolve tissue elements, prevent coagulation of the blood, dissolve yeasts and bacteria, and occasion other extraordinary reactions. Some of these activities, like that of antitoxin upon toxin, are direct, but others, such as those engaged in the solution of cells, are indirect —*i. e.*, accomplished through the intermediation of some third body. There seems to be no doubt but that the cell-solvents formed by the repeated introduction of this or that kind of cellular tissue into the body, and known as *cytotoxins*, are to play an important part in explaining many not now understood pathologic phenomena. It, therefore, becomes necessary to devote some attention to them, taking first the antimicrobic or bacteriolytic activity.

In various forms of forced immunity the blood may show, in addition to its antitoxic phenomenon, a new peculiarity in that it becomes *antimicrobic* or bacteriolytic, and so able to dissolve micro-organisms. Bacteriolytic serums are produced by the injection of the bacteria in living or dead culture. Like the other anti-bodies, they are specific. That is, they are solvent solely or chiefly for the particular bacteria used to excite their formation. They are, therefore, specific cytotoxins active upon bacteria. The actual solution of the cells caused by bacterial and other cytotoxins seems to be accomplished by a substance always present in the normal blood, and variously known as the *complementary body*, *alexin*, *cytase*, *lysin*, or *addiment*. This is, however, unable to act except in the presence of another body whose presence may result solely from experimental manipulation, and is variously called *amboceptor*, *immune body*, *substance sensibilisatrice*, *desmon*, *fixateur*, etc. It is, in reality, this body only that is produced in consequence of the immunization, but its presence is the occasion of the solvent action exerted by the complementary body or alexin. The specific cytotoxic serums have not yielded practical therapeutic results, as have the antitoxic serums, because no means has yet been devised to increase experimentally the complementary body by whose coöperation alone they can become active.

Immunity may be destroyed and the immune animal made susceptible. Immunity seems to depend largely upon the vital condition of the animal. Those in feeble health, exhausted, starved, etc., become more and more susceptible to disease. Not only do they become more susceptible to infection, but also to intoxication. Glycosuria, experimentally produced, is found to be very destructive to immunity. Sometimes mixed infections are followed by disease and death, when either micro-organism given alone might easily be overcome.

The relativity of immunity has already been discussed, and the fact that no sharp line between immunity and susceptibility exists has been pointed out. It, therefore, becomes apparent that variations in the virulence of the micro-organism may have the greatest influence upon immunity. Where there is a feebly virulent organism, immunity may seem to be a fact ; though when the same organism is examined in an exalted degree of virulence, the immunity is absent. Thus, the rabbit readily resists anthrax vaccines I. and II., the first fatal for white mice, the second fatal for guinea-pigs, but succumbs to more virulent anthrax bacilli. Combinations of bacteria may fail to kill susceptible animals because their metabolic products may neutralize each other, or because one may absorb with avidity certain elements necessary to the other or excrete some product inhibitory or destructive to the other, so that the variation of the micro-organisms alone will have great influence upon immunity.

Explanation of Immunity.—Immunity has not yet been satisfactorily explained. The modern theories teach that immunity depends upon *phagocytosis* or the destruction of microparasites and their toxins by phagocytes or upon the chemical action of the body-juices. The best explanation is contained in the so-called "lateral-chain theory" of Ehrlich.

The lateral-chain theory of immunity is one of the most pregnant hypotheses that has been introduced into medical science, and enables us to represent, with reasonable accuracy, certain operations of the body of which in the past our ideas were most chaotic. It is based upon the phenomenon of cellular nutrition, and supposes that the cells possess specific affinities for particular nutrient molecules through "*receptors*" or hypothetic appendages similar to the lateral chains of chemical molecules. These receptors or combining or fixing processes are peculiar in that they are capable of uniting only with molecules possessing corresponding combining appendages or "haptophores." The cellular nutrition is supposed to go on continuously through combinations formed by the union of haptophores and receptors. Certain toxic or otherwise active substances are supposed now and then to possess haptophores corresponding to the receptors of certain cells, and in this manner are able to attach themselves to the cells and act upon them. It has thus been demonstrated that tetanus toxin has such a power of combining with the cells of the central nervous system. When such a combination is made, two possibilities arise—either the cell is prevented from maintaining its nutrition because of the exclusion of the appropriate molecules by the attached molecules of the strange compound, or the attached

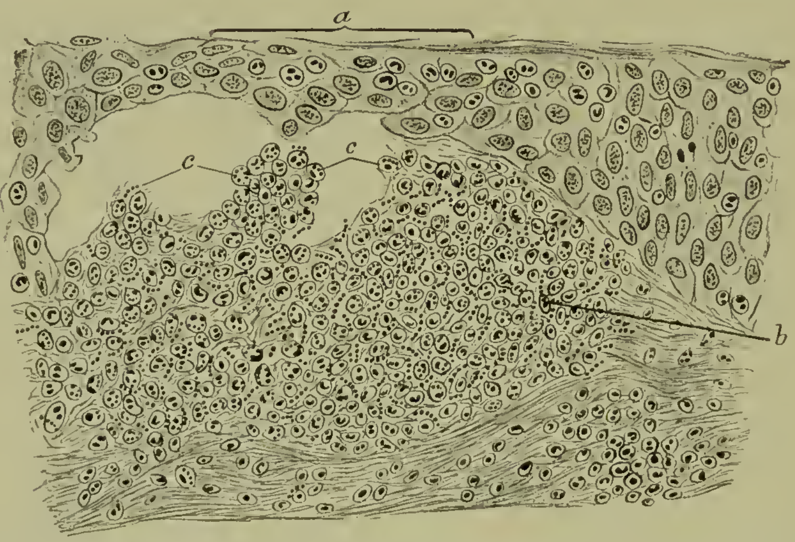

FIG. 201.—Erysipelas of the eyelid: *a*, Epithelial layer invaded by occasional leukocytes; *b*, invasion of subepithelial tissue by streptococci and leukocytes; *c*, *c*, streptococci inclosed in leukocytes (Weichselbaum).

molecules may themselves act upon the cell with stimulating, intoxicating, or fatal effect. This explains why certain animals lacking the appropriate receptors fail to experience ill effects from administered toxins, and so explains natural immunity.

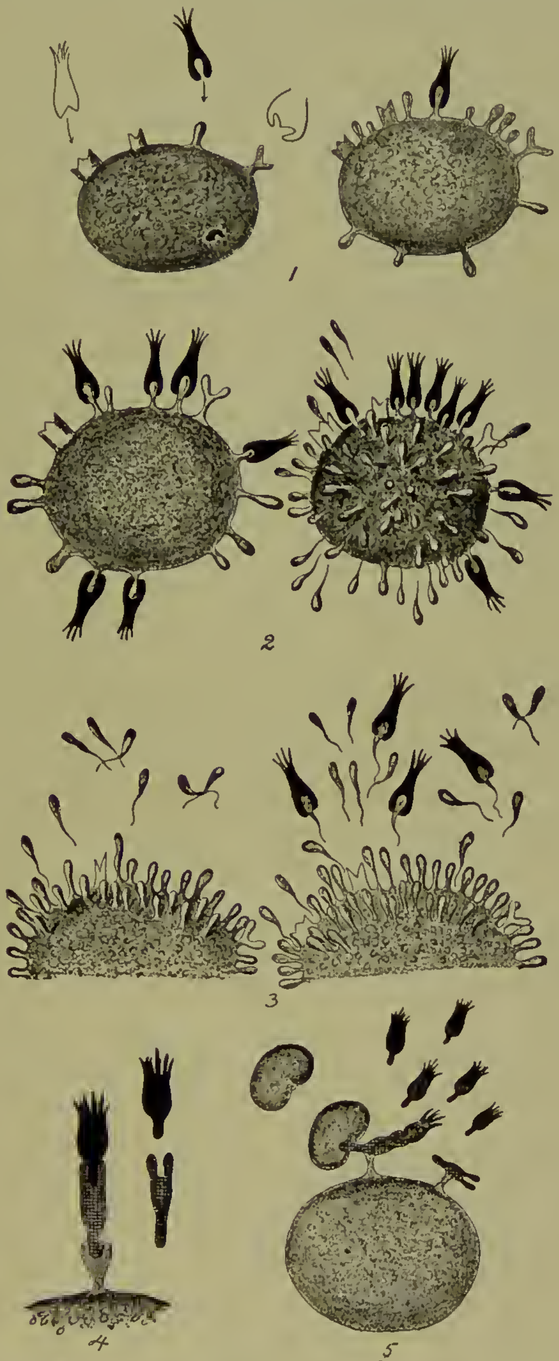

FIG. 202.—Diagrammatic representation of Ehrlich's lateral-chain theory of immunity: 1 shows a normal cell with its various lateral chains; in 2 is shown the union between receptor and haptophore; 3 shows liberated receptors; 4 and 5 show indirect union by means of the intermediate body or amboceptor (Ehrlich, Croonian Lecture, *Proc. Royal Society of London*, 1900, vol. lxvi., p. 437).

If the cell is not overcome by having its receptors occupied by the foreign haptophores, it may regenerate new receptors and then possess so many receptors as to permit the attachment of many more haptophores should the foreign substance again present itself. The more numerous the combination of haptophore and receptor, the greater the number of receptors that would be regenerated. Acquired immunity probably depends upon the increased number of receptors, by which a greater quantity of specific poison can be disposed of. If through repeated stimulation the regeneration of receptors becomes excessive, they may be liberated from the cell and circulate in the blood, still retaining the ability of combining with the appropriate haptophores.

The formation of *anti-bodies* is thought to depend upon the presence of large number of receptors in the blood of the repeatedly stimulated animals whose cells have been compelled to regenerate enormous numbers of receptors, that are subsequently discharged into the blood. Thus the lateral-chain theory explains natural immunity through the absence of appropriate receptors, acquired immunity through regeneration of receptors, and anti-body formation through the liberation of excessive receptors into the tissue juices.

CHAPTER X.

INFECTION AND THE INFECTIOUS DISEASES.

INFECTION.

Infection is the successful invasion of the body by parasites. It may refer to the habitual presence of bacteria upon the skin, in the nose, mouth, intestine, vagina, ear, etc., or it may refer to the occasional invasion of the tissues by bacteria whose accidental entrance and successful invasion are succeeded by disturbances, local or general, immediate or remote, caused by their metabolic products, or it may refer to the presence of worms or other larger parasites.

The almost ubiquitous distribution of microparasites of all kinds, the fact that many are regular tenants of the human body, and the remarkable activities of the bacteria, combine to make them the most common, as well as the most important, infecting parasites, and to narrow down the meaning of the word "infection" to invasion by bacteria.

Infection may depend upon microparasites regularly living at our expense upon the skin, in the bowel, and in the moist superficial cavities and apertures of the body. Such are, for the most part, harmless under all circumstances, but may become troublesome and even fatal should their activity be unusually stimulated, or should the resisting power of the host be reduced, or should some point of diminished resistance present itself, or infection may depend upon the operation of entirely foreign organisms that accidentally enter and establish themselves in the body.

The ability of a micro-organism of either class to endure the defensive mechanism set in operation by the body determines that it is *pathogenic* or disease-producing. Pathogenesis depends, however, upon varying peculiarities of the organism, its products, the tissues invaded, and the condition of the host. Certain organisms and groups of organisms seem to invade the body more frequently than others, their recurring appearance being characterized by lesions of sufficient uniformity to establish a type of infection or even a special disease.

Microparasites with similar metabolic products usually produce similar lesions, the most frequently observed being an actively chemotactic body that leads to suppuration. When a diseased condition, such as suppuration, results from the activity of any one of a number of organisms, it is said to be *non-specific;* when it results from the activity of but one organism, it is *specific*, as tuberculosis, leprosy, etc.

These principles will become more evident as the particular diseased conditions and their parasites are considered.

INFECTIOUS DISEASES CHARACTERIZED ESSENTIALLY BY LOCAL MANIFESTATIONS OF ACUTE FORM.

INFLAMMATION.

Inflammation is the sum of the phenomena manifested by an injured tissue. The phenomena are, for the most part, reactionary and reparative; some are destructive and disintegrative.

Originally applied to what was supposed to be a definite disease whose cardinal symptoms were "dolor, color, rubor cum tumor," the advance of knowledge has entirely changed our conception of it, and an investigation into its minutiæ forces us to admit that there are included in inflammation many closely related but entirely dissimilar processes. Inflammation has at present very little to do with "burning," and, like "malaria," the term no longer properly describes the condition to which it is applied. It is unfortunate that custom prevents us from casting it aside altogether and discussing the phenomena in particular, instead of in general.

Etiology.—Inflammation depends upon any kind of injury or damage. In the great majority of cases it is caused by micro-organisms infecting the tissues, and the frequency with which infection accompanies inflammation has led some to the erroneous assumption that inflammation must always depend upon bacteria.

Inflammation may be *infectious* or *non-infectious*. The former are frequent; the latter, comparatively rare.

Non-infectious inflammations may be caused by traumatic injuries, such as contusions, burns, blisters, etc., the application of croton oil and other irritants, or the introduction of certain bacterial products. Their lesions are identical with those of the infective variety, except that bacteria are absent.

Non-infectious inflammations readily become infected from the body surfaces, upon which bacteria always occur, and many of the cases in which bacteria were found in what should have been non-infectious lesions can be explained as artefacts depending upon secondary infection.

Bacteriology of Inflammation.—There is no specific bacterium of inflammation, although a few common organisms which occur alone or together in the majority of suppurations are sometimes erroneously so called. In order that a bacterium shall be pyogenic, all that is necessary is that it be able to maintain a parasitic existence and have chemotactic products. The micro-organisms most frequently observed in suppuration are external parasites of the body, and are common upon its surfaces, in its various recesses, and in the alimentary canal. A few, however, are strangers and are admitted accidentally.

The common organisms of suppuration are Staphylococcus pyogenes aureus, Staphylococcus pyogenes albus, and Streptococcus pyogenes. The rarer organisms are the gonococcus, the typhoid and the colon bacillus, Bacillus pyocyaneus, Bacillus proteus vulgaris, Bacillus tuberculosis, and Bacillus mallei.

Staphylococcus pyogenes aureus is commonly found upon the skin, in the mouth, upon the conjunctiva, etc. It is possible that under normal conditions it is devoid of virulence, and acquires pathogenic properties only when abnormal conditions arise. It is the most frequent organism found in superficial suppurations.

The organism is spheric in shape, and measures about 0.7 μ in diameter. As no definite arrangement of the cocci exists, they gather together in irregular clusters and are so found in the pus and in the tissues. Cocci that are about to divide are somewhat larger than the others and slightly ovoid in shape. No spores or flagella are observed, and the organism is not motile.

The staphylococci stain well and are beautifully colored by Gram's method. They grow luxuriantly between 18° and 39° C., upon all the artificial media, the only characteristic of their vegetation being what is described as a "golden-yellow" color, but which is usually a faded yellow color. The pigment formation is perhaps best seen upon potato. The staphylococcus liquefies gelatin through an enzyme, and in puncture cultures produces a long, tapering, tubular liquefaction. It coagulates milk and digests the casein which it contains.

The recognition of the organism is easy if its source is known, but difficult otherwise, as nearly all its peculiarities are shared by other micro-organisms.

The pathogenesis of Staphylococcus aureus is variable. When freshly isolated from pus, it readily kills rabbits and other animals by pyemia or septicemia. In these cases it is found in the blood vessels in the form of micro-organismal emboli, or, if the animal lives longer, in the small abscesses to which these emboli give origin. The coccus has been shown by experiment to be pathogenic for man, furuncles having resulted from rubbing it into the skin, and abscesses from its deeper inoculation. When admitted through accidental punctures of the fingers into which it has entered, it has caused most dangerous lesions.

From insignificant lesions of the surface it may be embolically admitted into the circulation and produce endocarditis, ostitis, periostitis, osteomyelitis, peritonitis, pericarditis, etc.

Staphylococcus pyogenes albus may be a colorless form of the Staphylococcus aureus or may be a separate species. It differs from its relative only in the absence of the yellow pigment formation. In all probability the white staphylococcus is less virulent, and consequently less dangerous, than the "golden staphylococcus." The two species are not infrequently associated, and, in general, what has been said of the Staphylococcus aureus applies equally to the Staphylococcus albus.

Staphylococcus epidermidis albus is not infrequently found in dermal suppurations, but as this organism is habitually present upon the skin and readily grows on media of all kinds, its presence in pathologic lesions may be accidental. On the other hand, it may be that it is the cause of many of the lesions, and hence is an organism of immense importance to the surgeon. In its morphologic, cultural, and tinctorial peculiarities it resembles the other staphylococci, and inasmuch as it produces no color, particularly resembles Staphylococcus albus.

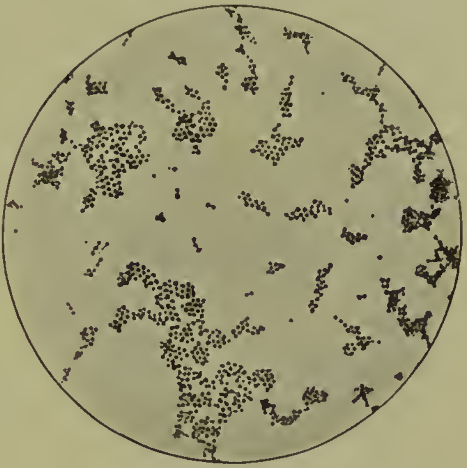

FIG. 203.—Staphylococcus pyogenes aureus from an agar-agar culture (× 1000) (Günther).

Streptococcus pyogenes is one of the most important and most dangerous micro-organisms. It is frequently found in suppurations, although it is not so common as the staphylococcus. The natural distribution of the organism is somewhat uncertain. Many streptococci are known to exist in nature, and many are common in diseases and in suppuration in animals. Some are found in the mouth, others in the intestine of man. A streptococcus identical with Streptococcus pyogenes in morphologic, cultural, and tinctorial peculiarities, has been found by Fehleisen in erysipelas of man, and has been called Streptococcus erysipelatis. It is probably identical with the original Streptococcus pyogenes of Rosenbach.

The streptococcus is a spheric organism measuring from 0.5 to 1 μ in diameter, and arranged in rows to which the terms "rosary," "string of beads," etc., have been applied. The number of cocci contained in one of the chains varies enormously. At one time an attempt was made to divide the streptococci in various species according to the length of the chains, the **Streptococcus brevis** having short chains, the **Streptococcus longus**, long chains. It was also supposed that the shorter chains facilitated the ready transportation of the micro-organisms through the currents of body fluids, hence that a streptococcus that grew in this form was much more virulent than one whole long chain which could, with difficulty, be disentangled and transported.

There seemed to be no validity in this differentiation, and it has been abandoned. Whether all streptococci are identical or only closely related is not known.

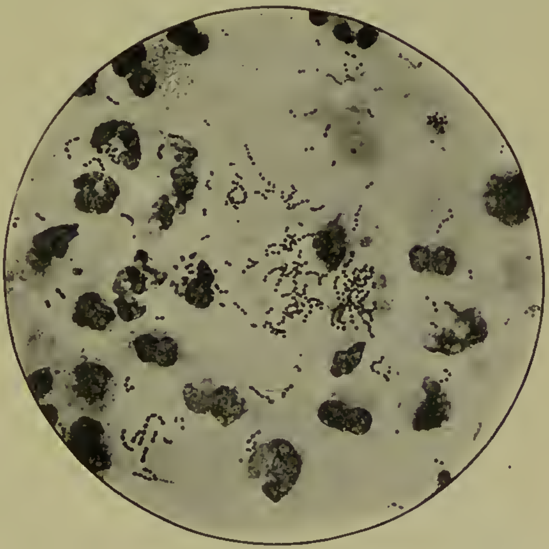

FIG. 204.—Streptococcus pyogenes from the pus taken from an abscess (× 1000) (Fränkel and Pfeiffer).

The organisms produce no spores, have no flagella, and are not motile. They color well with ordinary solutions of the anilin dyes and by Gram's method. They do not liquefy gelatin.

The streptococcus grows upon most of the artificial media, but its growth is delicate. Upon obliquely solidified gelatin, agar-agar, and blood-serum it appears in the form of little dewdrop-like, circular, scarcely elevated colonies, which attain their full size in about twenty-four hours at 37° C. The colonies never become confluent so as to form a mass. In gelatin no liquefaction occurs. In bouillon the streptococcus produces either a diffused cloudiness or a flocculent sediment. What governs this is not known, but some have thought it well to divide the cultures into diffuse and conglomerate forms—Streptococcus diffusus, Streptococcus conglomeratus. Milk is coagulated and digested by the streptococcus.

The organism produces acids and grows quite well in acid media. The temperature at which it grows is rather high, its best development always being at about 37° C. It is killed at 55° C.

The vitality of the organism is low, and upon most media the cultures must be frequently transplanted or they die. When kept in gelatin or agar-agar punctures, they live longer than when cultivated upon the surface.

Like the staphylococci, the recognition of the streptococcus is easy if one knows the source from which it is obtained. In the absence of this information, however, it may be impossible to determine that a given culture is the Streptococcus pyogenes hominis.

This is the more true inasmuch as the virulence of the organism is remarkably variable. It is peculiar in being pathogenic for a certain animal and not for others. Thus, because a streptococcus has been isolated from a fatal case of human infection is no guarantee that the culture will be virulent for mice, guinea-pigs, or rabbits. The reverse may also be true, and a streptococcus highly virulent for rabbits may not injure man or horses. It even seems true that when permitted to colonize in the animal body, it develops a selective tendency for those tissues in which it has previously colonized most successfully.

In consequence of these peculiarities, the effects produced by the streptococcus vary greatly under both natural and experimental conditions. In the throat the streptococcus grows readily and sometimes produces a fibrinous inflammation closely resembling diphtheria. From this throat lesion it may be absorbed into the circulation and occasion a deep suppuration. Admitted to an external wound, it may cause an ordinary abscess, a phlegmon, or erysipelas.

When introduced into mice, streptococci which have been recently isolated usually cause death from septicemia; in guinea-pigs they may also cause septicemia. When introduced into the ear vein of a rabbit, they may cause death from septicemia in a day or two, or occasion pyemia, if death is delayed. When rabbits are inoculated subcutaneously upon the ear, erysipelas commonly results.

The virulence of the streptococcus for any particular species of animal can be maintained by frequent passage through animals of that species. Marmorek declares that attenuation takes place during the intermediate artificial cultivation, and has recommended certain media upon which this does not occur. The immunization of animals to the streptococcus is attended with little difficulty. The serum of animals immunized for a long time is bacteriolytic, and can sometimes be successfully employed for treating streptococcus infection.

In human pathology the streptococcus has been observed in suppuration, erysipelas, ulcerative endocarditis, periostitis, ostitis, otitis, meningitis, emphysema, pneumonia, lymphangitis, phlegmons, sepsis, puerperal endometritis, infantile enteritis, and pseudomembranous angina. By some pathologists streptococci are regarded as the cause of scarlatina.

The Gonococcus of Neisser.—This is a minute diplococcus which does not seem to occur in nature except in gonorrhea.

Morphology.—The organism always occurs in the form of a diplococcus. The classic description is that it resembles the German biscuit called a "Semmel"; as this expresses but little to those unfamiliar with the delicious "brödchen," it may be well to add that in shape it is much like a coffee-bean, the two cocci having the approximated surfaces flattened—sometimes even appearing concave. Each organism measures about 1 μ in diameter. No spores are formed, there are no flagella, and the organism is not motile. It stains with the aqueous solutions of the anilin dyes, but not by Gram's method.

Cultivation.—The gonococcus can be cultivated from the creamy pus of gonorrhea and from other of the secretions upon a mixture of blood-serum and agar-agar. Human serum is best adapted to the purpose. An equal quantity of it and of melted agar-agar can be poured into a sterile Petri dish, mixed, and allowed to solidify. The pus is taken up with a platinum wire and inoculated by a series of parallel strokes. The colonies of gonococci grow at a temperature of 37° C., and appear after twenty-four hours as small, grayish, translucent points. Successful transplantation is difficult, as the vitality of the organism readily wanes upon artificial media. The appearance of the colonies upon the primary culture, their failure to grow upon frequent transplantation, their morphology, and their refusal to retain Gram's stain are characteristic.

Pathogenesis.—The gonococcus is pathogenic for man, and excites a very acute inflammation when its foothold is once secured upon an epithelium of the squamous type. It, therefore, causes urethritis, vaginitis, cystitis, balanitis, posthitis, conjunctivitis, stomatitis, etc. Its ability to invade columnar epithelia is doubted by some, but the fact that gonorrhea in men may be complicated by vesiculitis and orchitis, and in women be accompanied by or succeeded by endometritis, salpingitis, and oöphoritis, may indicate it. It is thought by some that these latter lesions, instead of being caused by the gonococcus itself, are dependent upon staphylococci and streptococci, which readily invade the tissues denuded by the gonococci.

Gonorrhea is chiefly observed in the form of urethritis, transmitted by sexual intercourse, although the infectious organisms may be carried to other parts of the body by the fingers, etc. It is usually a local infection which spreads from part to part by contiguity and continuity of tissue. It may in rare cases distribute by blood metastasis, and gonorrheal endocarditis has been observed in a few cases. A case of this kind which I studied was found, in spite of the gonorrhea and associated orchitis, to have endocarditis depending upon another much larger diplococcus, which stained by Gram's method.

Though the virulence of the gonococcus for man is very marked, it is not pathogenic for animals. Intentional inoculation of the human urethra has successfully produced gonorrhea, but with the exception of a few unconfirmed observations, no claims of successful animal inoculation have been made.

Bacillus pyocyaneus is frequent upon the human skin, and not infrequent in suppurative conditions. It is thought by some to be instrumental in the production of the lesions in which it occurs; by others it is supposed to be a harmless saprophyte that enters the wound from the contiguous skin. It is usually found in association with other organisms, although occasionally alone. It is not uncommonly found in the throat in suspected diphtheria cultures, and sometimes in cases of diphtheria.

Morphology.—The bacillus is very small and delicate, sometimes rounded, sometimes somewhat pointed at the ends. It measures about 1 to 2 by 0.3 μ, is actively motile, and has a terminal flagellum which can be demonstrated by Löffler's method. No spores are produced. The bacilli usually occur singly, although sometimes two are joined. No long filaments are formed.

Staining.—It stains readily with ordinary solutions, but not by Gram's method.

Cultivation.—The Bacillus pyocyaneus is readily cultivated upon all artificial media, and although it forms no spores, the cultures can readily be kept for long periods. It is most readily secured from the blue or blue-green pus in which it occurs by the plate method, the colonies appearing early as small, thin, granular dots which, under the microscope, show a finely granular periphery and coarsely granular center. Liquefaction of the gelatin begins shortly, and each colony becomes surrounded by fluid, its granular edges melting away as the motile bacilli detach. The bacillus is both aërobic and anaërobic. When planted in gelatin punctures, the bacilli grow all along the line of inoculation and upon the surface, causing the formation of a long narrow funnel at first. This soon widens as the gelatin liquefies, and the fluid becomes more and more turbid from the development of the bacteria. The gelatin surrounding the liquefaction becomes green and fluorescent. Ultimately, all the gelatin becomes fluid, turbid, and contains flocculi which finally sediment, forming a greenish slime.

Upon agar-agar the growth is luxuriant all along the stroke of inoculation, and forms a grayish-green, dry, somewhat metallic film. The agar-agar beneath this—and after a day or two all the agar-agar in the tube—becomes greenish. The green color is at first bright, but in a short time becomes bluish, and as time passes becomes very dark—almost black as the blue-green color deepens. Sometimes instead of the blue-green color a brownish or reddish-brown color develops. Whether the color of the agar-agar be reddish-brown or blue-green, the grayish band formed by the growth stands out in contrast.

Upon potato the growth forms a greenish, rather dry, mass, about which the potato may become bright green, although it often simply darkens.

Upon blood-serum the growth is green. On coagulated white of egg it is sometimes bright green, sometimes merely dirty in appearance. In peptone solution the bacillus may form a bright blue color, but this also often fails, the solution simply becoming discolored.

Chemistry.—The blue color depends upon a ptomain known as pyocyanin; the green color, upon fluorescin. The blue pigment usually predominates.

The bacillus also produces an enzyme by which its own dead are dissolved, and by which it is said other bacteria, and probably other cells, can be dissolved.

Pathogenesis.—When freshly isolated, the Bacillus pyocyaneus is pathogenic for the lower animals. When virulent cultures are injected beneath the skin of the guinea-pig or rabbit, they cause local suppuration, soon followed by septicemia, from which the animal dies. Introduced into the peritoneal cavity, it causes fibrinous and purulent peritonitis, with fatal septic infection.

Its pathogenic action in man, as has already been said, is uncertain. It has been found in the saliva, sputum, and sweat of comparatively healthy persons, and as a saprophyte in the stomach. It is commonly found in suppurating wounds and in tuberculous cavities. It has frequently been observed in purulent otitis, and is occasionally observed in pericardial effusions, diphtheric angina, meningitis, bronchopneumonia, diarrhea, dysentery, and in some cases of generalized infection.

Bacillus Proteus Vulgaris.—This organism, which was first observed by Hauser as a saprophyte in a decomposing animal infusion, and which seems to be rather widely distributed in nature, occasionally presents itself unexpectedly in infectious and pyogenic lesions.

Morphology.—The organisms are distinctly bacillary in form, although somewhat pleomorphous, and hence called proteus. The rods may be very short, but occasionally grow into longer threads. The organism measures about 1.2 to 4 by 0.6 μ. No spores are formed. It is actively motile, and has flagella arising in large numbers from every part of the surface.

Staining.—It stains readily by the ordinary methods, but fails to stain by Gram's method.

Cultivation.—The organism grows well upon all the ordinary media. The colonies which form upon gelatin plates are peculiar in that they are extremely irregular in outline, and consist of actively motile filaments of bacilli which keep changing the shape and position of the colony that can truly be described as motile and ameboid. This ameboid movement of the colonies is best observed in thinner gelatin than that usually employed in bacteriologic work.

Puncture cultures in gelatin show a rapid tubular liquefaction that is not at all characteristic.

Upon the surface of agar-agar a moist, smooth, thin, shining, transparent, slightly grayish layer is formed. It is rarely ever luxuriant, and does not reach the sides of the tube. On potato the growth forms a dirty discoloration.

Chemistry.—Milk is coagulated by the bacillus. Dextrose and sucrose are fermented. Indol and phenol are formed in peptone-containing media. Nitrates are reduced to nitrites, and then partly to ammonia.

Pathogenesis.—The proteus is possessed of very feeble pathogenic properties. In animals large doses sometimes cause abscesses. Very large doses of fluid cultures seem to kill through intoxication. In man the proteus probably never infects the normal body, but in diseased tissue it is sometimes able to secure a foothold. It has thus been secured from wound and puerperal infections, purulent peritonitis, endometritis, etc. It also sometimes grows in the bladder, causing cystitis, pyelitis, and even nephritis. It has also been found in acute infections, acute febrile jaundice, or Weil's disease.

The pneumococcus, meningococcus, typhoid bacillus, colon bacillus, tubercle bacillus, and other pathogenic organisms more rarely associated with suppuration will be described in more appropriate chapters.

Classification.—Inflammations may be *acute* or *chronic.*

Acute inflammation is rapid in onset, brief in duration, and destructive in tendency.

Chronic inflammation is insidious in onset, protracted in duration, and characterized by progressive, productive lesions that show no tendency to recover. This process is entirely different from anything embodied in the original conception of inflammation. An inflammatory condition not distinctly acute or chronic is frequently described as *subacute.*

According to the distribution it is customary to speak of—

Parenchymatous inflammation, which affects the essential functional cells of an organ.

Interstitial inflammation, which affects the supporting connective-tissue framework or stroma.

Cartarrhal inflammation which affects the epithelial surfaces of the body, the ducts of glands, or the walls of the air-cells of the lung. It is characterized by changes in the cells and superficial exudation. When catarrhal inflammation is characterized by desquamation of the epithelium, it is known as **desquamative inflammation.**

According to the form of exudation or tissue change by which they are accompanied, inflammations are described as—

Vesicular or **herpetic,** when characterized by the formation of small vesicles or blisters filled with serous fluid, as in herpes.

Pustular, when, as in small-pox, furuncle, etc., there are small elevations filled with pus upon the surface.

Diphtheric or **croupous,** when the surface is covered with a pseudomembrane formed of fibrin and degenerated cells.

Ulcerative, when characterized by the loss of some of the inflamed tissue by suppuration, necrosis, or gangrene.

Degenerative, when an unusual tissue degeneration occurs.

Adhesive or **agglutinative,** when the tendency of the process is to form fibrous unions between contiguous parts.

Gangrenous, when associated with gangrene.

Suppurative, when culminating in suppuration.

Phlegmonous, when the cellular tissue becomes infiltrated with pus.

Productive, when chronic and tending toward hyperplasia of connective tissue.

Exudative, when characterized by excessive or peculiar exudates, as the pleuritic effusion and diphtheric membrane.

Specific, when caused by definite micro-organisms.

Phenomena of Inflammation.—The clinical manifestations by which inflammation was originally recognized were *pain*, *heat*, *redness*, and *swelling*.

Pain.—The pain, which is severe in acute inflammations, depends chiefly upon the pressure exerted upon the nerve-endings by the accumulated products. It is possible that the pain depends in part upon the chemic effects of the bacterial products,—toxins, acids, enzymes, etc.,—upon the nerve-endings as well as upon the pressure. It is most severe where the tissue is unyielding, as in the whitlow, or felon, which occurs upon the finger in the unyielding fascia through which the nerves of touch pass. Inflammations of loose cellular tissue may be accompanied by little pain. In chronic inflammation pain may be absent.

Heat.—The elevation of temperature characteristic of acute inflammation depends upon active hyperemia, by which an increase of hot arterial blood reaches the part, and possibly in part to increased combustion taking place in it.

Redness.—The red color depends solely upon the arterial hyperemia and increased number of red vessels.

Swelling.—The swelling at first depends upon the hyperemia and is commensurate with it. As the inflammation progresses, however, a new factor, the *exudate*, makes its appearance and becomes of paramount importance.

Loss of Function.—An organ or tissue in which active hyperemia is in progress; in which the resulting swelling becomes painful, in which nutritional changes are in progress, and into which an inflammatory exudate takes place, is one in which the performance of function must be interrupted.

Acute Inflammation.—The alterations that take place in irritated tissue can be studied in detail in a microscopic preparation made by spreading the withdrawn mesentery of a living frog or other small animal over a cork ring. The exposure to the atmosphere is itself sufficient to occasion inflammatory reactions in the delicate tissue. It was by this method of examination that Cohnheim first succeeded in discovering the origin of the inflammatory cells.

1. **Vascular Phenomena of Inflammation.**—In all the higher animals these are constant, although they do not in themselves constitute inflammation. That they are not the essential phenomena is shown by the fact that phenomena analogous to inflammation can take place in animals that have no vascular system. The changes occur in the following order:

1. A momentary spasm in the blood vessel as the irritant is applied to it.
2. Relaxation and dilatation of the arterioles, with increased rapidity of the current.
3. Further increase in the dilatation of the arterioles, with marked slowing of the current. In the arterioles and venules through which the blood has been passing so rapidly that corpuscles cannot be observed, except as a central solid stream of red between which and the vessel-wall clear plasma with occasional leukocytes could be seen, the corpuscles now become distinctly visible, because of the slowness of their movement, and distribute themselves throughout the plasma. It may be that the endothelial cells become altered at this time, for the future behavior of the leukocytes seems to show them to be abnormally sticky.
4. Transmigration of leukocytes. The leukocytes, of which but few were previously visible, occur in unusual numbers and adhere to the walls of the vessels. At this time it becomes impossible any longer to differentiate between the phenomena of the vessels and the phenomena of the cells. Should one of the leukocytes adhering to the vessel-wall be carefully watched, a small bud of cytoplasm can sometimes be seen projecting through the vessel-wall into the surrounding perivascular tissue, as though a portion

of the leukocyte had pushed its way through one of the stigmata of the vessel. It is, of course, not impossible that it is actually projecting through one of the endothelial cells lining the blood vessel. As time goes on this little bud becomes larger and larger; the nucleus is observed to be partly within and partly without the vessel, and soon the whole nucleus finds itself outside the vessel, with only a small protoplasmic attachment, and not very long after the beginning of the observation the cell will have completely passed through the wall of the vessel, the whole process taking about twenty minutes.

The passage of the white corpuscles through the walls of the vessels is called *diapedesis* or *transmigration*. It is perhaps better to use the word transmigration exclusively when the escape of leukocytes is meant, as diapedesis is a convenient term by which to indicate the escape of erythrocytes from the vessel. Prior to and during the escape of the leukocytes we find an increased amount of transudate passing from the vessel into the tissue, so that its lymphatic spaces are unusually dilated, and prepared to receive the leukocytes which escape.

Transmigration is an active and purposeful phenomenon, the leukocytes leaving the blood vessels in response to some strong external stimulus to which the name *chemotaxis*, *chemiotaxis*, or *chemotropism* is applied. The cells which transmigrate are chiefly polymorphonuclear leukocytes, and are both phagocytic and ameboid.

2. **Phenomena of the Lymphatic Apparatus.**—These are largely secondary to the phenomena of the blood vessels. The increased transudation of fluid from the hyperemic vessels causes the lymphatic spaces of the tissue to become distended with fluid, so that the tissue becomes edematous. The transmigrated leukocytes find themselves in the enlarged interstices of an edematous tissue, in which ameboid movement is greatly facilitated.

The transmigrated leukocyte seems to be a general scavenger. In many infectious processes the leukocytes energetically attack and destroy the bacteria. In erysipelas, in which the lymphatic spaces contain chains of streptococci, the leukocytes attack the bacteria, and apparently prey upon them. Whether or not the bacteria are destroyed through their agency is an open question, but be that as it may, the bodies of the leukocytes are found to contain the bacteria. These transmigrated leukocytes are, therefore, active phagocytes.

Many of the cells die; others, having accomplished their purpose, are carried by currents of fluid to the lymph-channels and then through the vessels to the neighboring lymphatic nodes. It is not known how many of the transmigrated leukocytes ever again reach the blood.

Should the severity of the inflammation be great, and the destruction of tissue considerable, the number of transmigrated leukocytes collected in the tissues may become so great as to effect its disorganization by obstructing the lymphatic currents, filling up the interstices, and appropriating the nutriment intended for the essential cells of the tissue, by pressing upon the tissue leading to atrophy and disintegration, and by digesting its macerated and compromised elements through cellular enzymes.

3. **Phenomena on the Part of the Tissues Affected.**—That the cells of inflamed tissues were apt to multiply, as evidenced by the many karyokinetic figures in their nuclei, was first observed by Virchow, who consequently attributed inflammation to hypernutrition. It is not now conceded that inflamed tissue is hypernourished. It is, however, irritated, and in consequence stimulated, and the cells probably multiply because they are stimulated rather than because they are overnourished. The importance attributed to the multiplication of the cells of the tissue by Virchow has been largely annuled by the observations of Cohnheim. Virchow's original idea was that

all the cells of inflammatory exudates resulted from multiplication of the cells of the tissues, but Cohnheim's observation that the cells transmigrate from the blood vessels into the tissue makes it evident that the changes in the cells belonging to the tissue are of secondary importance.

The important change in the inflamed tissue is its invasion by the leukocytes, which, according to the degree of inflammation, riddle it with their ever-increasing numbers, and bring about the damage described above.

The body being constructed on the most economic plan possible, does not provide that any tissue shall be so well supplied with nutriment that it can maintain the vitality of its own cells, plus an invading army of leukocytes. Hence so soon as a considerable accumulation of leukocytes occurs in a tissue, evidences of malnutrition, evinced by degeneration of the normal tissue elements, can be seen. A very large number of leukocytes in a tissue invariably occasions its dissolution or colliquation, with the formation of a more or less circumscribed cavity of indefinite size and shape, filled with a creamy, sometimes slightly blood-stained, material, which, upon microscopic examination, is shown to be made up of leukocytes, various destroyed tissue cells, and molecular matter. Such a circumscribed cavity is called an *abscess*, and the fluid it contains is *pus*. The process of pus formation is called *suppuration*.

The colliquation that takes place in suppurating tissue is not entirely due to disorganization or malnutrition. It depends in some measure upon tissue *digestion* by the transmigrated cells, as the transuded fluids seem to contain a proteolytic enzyme. Pus always contains albumoses, probably formed by the action of this ferment upon the infiltrated tissue. The ferment is probably produced by the cells and may be contained in their granules, as pus-cells always have solvent powers. The colliquation, while destructive, may, in reality, be a benign process, in that its tendency is to effect the ultimate removal of the cause of inflammation.

The formation of an abscess usually marks the termination of the inflammation; at least it does so in the sense that so long as the activity of the inflammation is marked, infiltration of the tissue continues in all directions, but so soon as the inflammation is localized or circumscribed, the formation of an abscess takes place.

Abscesses ultimately evacuate, their contents being discharged either from the surface of the body or into one of its cavities. The resulting space with suppurating walls then becomes an *ulcer*, which heals by the process known as organization, cicatrization, or healing. *Ulceration* is molecular disintegration of the tissues resulting from inflammation. It is usually applied to superficial lesions only. Any superficial denudation is termed an *abrasion*. If too large to heal at once or if infected, an abraded surface soon becomes *ulcerated* in consequence of the irritation of the air, of secretions dried upon the surface, of chemic changes in the dried juices, and infection. Evacuated abscesses are frequently so deep that they are described as *sinuses*, and superficial cavities following suppuration may have sinuses extending from them. If, in consequence of suppuration, ulceration, or injury, cavities of the body are caused to communicate with one another or with the exterior, the channel of communication is called a *fistula*. Such communications are frequent between the vagina and bladder and vagina and rectum in consequence of the traumatic injuries sustained during parturition.

The Products of Inflammation.—The products of inflammation are known as *inflammatory exudates*. They consist of the materials exuded from the blood vessels or developed in the tissues, and vary according to the severity and duration of the lesion. Considering them in the order of their complexity, they are:

1. **Serous Exudate.**—This characterizes the mildest form of inflammation, and being simply an increased transudate from the blood vessels, probably requires no alterations in their walls other than occur in hyperemia. Every inflammation has a certain amount of serous exudate, but certain of them, especially affecting serous membranes, are characterized by the accumulation of a considerable quantity of serum. Thus, in pleuritis, one not infrequently finds a liter or two of fluid in the pleural cavity, and in pericarditis the amount of pericardial fluid may be increased tenfold.

The serous exudate of inflammation is invariably more highly albuminous in nature than that of dropsy, and is prone to spontaneous coagulation when withdrawn from the body. When examined microscopically, it is seen to contain a larger number of leukocytes than are found in dropsical fluids.

2. **Fibrinous Exudate.**—This is characterized by the formation of fibrin. It may not differ materially from the serous exudate, except in the fibrin formed by its coagulation. Fibrin is formed by the coagulation of simpler exudates and by fibrinoid degeneration of certain cells. Fibrinous exudates are common in diphtheria and pneumonia, both of which diseases depend upon bacteria from cultures of which a fibrin ferment has been separated. It, therefore, becomes a question whether there is any real difference in the character of the exudate, or whether the fibrin formation is not merely the result of the action of the ferments upon ordinary exudates. The microscopic appearance of the fibrin will vary according to circumstances. In the alveoli of the lungs it can be seen when appropriately stained, and indeed, without staining, as delicate fibrilla among the cells—red and white blood-corpuscles—which fill the spaces. In the diphtheric membrane, instead of delicate fibrilla, more or less laminated masses appear upon the surface of the mucous membrane, with irregular flakes among the cells and fibers of the mucous and submucous tissues. Being upon the surface of the tissue, this diphtheric membrane, as it is called, may readily be stripped off, leaving an abraded surface upon which the conditions for the formation of a new similar

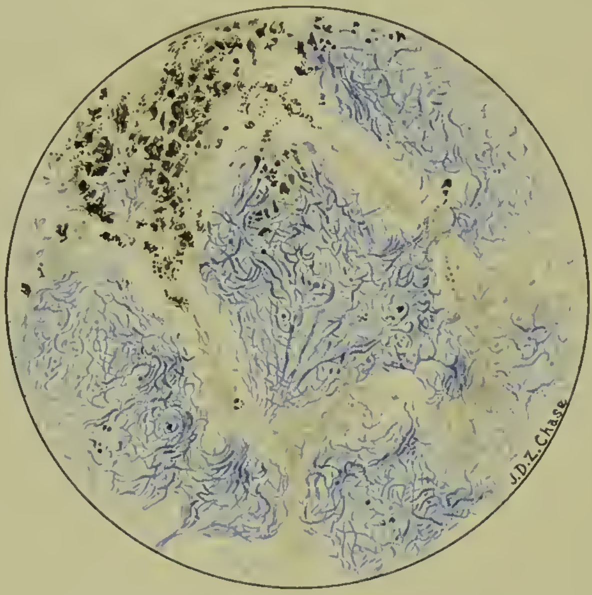

FIG. 205.—Croupous or fibrinous pneumonia, stage of red hepatization; stained by Weigert's method to show the fibrin only. The blue threads filling the air-cells consist of fibrin filaments (× 180).

membrane are most excellent. After having been formed for some time, fibrin not infrequently becomes granular.

Fibrinous exudates are frequently called *croupous*. Diphtheria is often called *croup*; fibrinous pneumonia, *croupous pneumonia*, and by some this use of the term croupous is even applied to a variety of nephritis in which tube-casts of a fibrinous nature are formed. Fibrinous exudates are usually quite destructive because of the inclosure of the epithelial cells in the coagulation mass.

3. **Hemorrhagic Exudate.**—This is one that contains erythrocytes. It usually indicates that the blood vessels have been injured. In inflammation hemorrhage by diapedesis is not at all uncommon, but where enough erythrocytes have escaped from the vessels to color the exudate red, the injury to the blood vessels has been of unusual extent. The regularity with which hemorrhagic exudates occur in certain diseases—pneumonia—indicates that some endotheliolytic poison is present.

4. **Corpuscular Exudate.**—The corpuscular exudate characterizes what is known as *round-cell infiltration*, *cellular exudation*, *purulent exudation*, and *suppuration*. It is an exudate composed essentially of transmigrated leukocytes. The cells may be few or many—so few that they are to be found only by microscopic examination in small groups here and there in the neighborhood of the blood vessels; or they may be so numerous as to cause liquefaction necrosis of the tissue, and the formation of abscesses holding a liter or more of pus.

The cells of the corpuscular exudate are chiefly polymorphonuclear leukocytes. These leukocytes being the most numerous and the most distinctly ameboid, can escape from the blood vessels with greatest facility.

5. **Pus** is the fluid contained in an abscess. It is an opaque, creamy, yellowish fluid, made up of *pus-cells* and *liquor puris*. It is usually alkaline, though sometimes acid in reaction, and has a specific gravity of about 1.050.

Laudable pus is the ordinary yellowish, creamy pus, seen in acute abscesses.

Sanious pus is slightly tinged with blood. *Curdy* or *cheesy pus* contains shreds or flakes of necrotic tissue. It usually occurs in deep abscesses of tuberculous origin, and is characteristic of *cold abscesses*. It may contain no pus-cells.

Ichorous pus is thin and acrid and excoriates the surrounding tissues with which it comes in contact. It usually depends upon putrefactive organisms that have entered after the abscess has evacuated.

Mucopus and *seropus* contain unusual quantities of mucus and serum respectively.

The pus-cells, when examined microscopically, appear spheric in shape, slightly larger than leukocytes, and granular. When treated with a dilute solution of acetic acid, the granules disappear, and a nucleus consisting of three lobes becomes distinct in the center of the cell. When stained with the Ehrlich dye, they show neutrophilic granules. Sometimes they contain droplets of glycogen. The pus-cells may be alive or dead, according to the age of the abscess, the length of time they have been retained within it, and the effects of the bacterial products with which they have come in contact. Living pus-cells, like leukocytes, are ameboid, and manifest the peculiar phenomena of ameboid movement and phagocytosis. When dead, the pus-cells undergo disintegration, and become transformed into molecular débris. In addition to the cells pus contains remnants of the destroyed tissue in which the abscess was formed. Occasional opportunities arise for practically applying this knowledge, as when abscesses of the liver discharge their contents through the respiratory passages, the diagnosis being possible by the discovery of liver-cells in the pus.

Bacteria are usually present in pus. Among those frequently observed we find Streptococcus pyogenes, Staphylococcus pyogenes aureus and albus, Bacillus coli communis, the typhoid bacillus, pneumococcus, gonococcus, etc.

Abscesses are called "*hot*" and "*cold*" by the clinician, according to the phenomena attending their development. The "hot" abscess results from the acute inflammation, while a "cold" abscess is a collection of semifluid matter slowly formed by tissue disintegration—such are seen in tuberculosis of the bones and in the degeneration of certain tumors.

Embolic abscesses depend upon septic emboli and characterize pyemia; hence they are also called *septic* and pyemic abscesses. They may be lymphogenic or hematogenic.

Suppuration may occur in any tissue of the body, except such ametabolic tissues as the hair, teeth, nails, etc. The ordinary resistant tissues of the body readily yield to the infiltration of the small round-cells and are destroyed. Abscesses ordinarily form in the softer tissues, but can with almost equal facility form in the densest ones. Abscesses of bone may form either beneath the periosteum or actually in the deeper structure of the bone, and usually begin in the neighborhood of a blood vessel. The outwandered leukocytes invade the Haversian system, enter the lacunæ, and bring about absorption of the earthy matter, the bone becoming unusually porous. Ultimately the osseous tissue may liquefy and become part of the purulent contents of the abscess. Such softening of the osseous tissue is known as *caries*, or rarefying osteitis. Cartilage is invaded similarly, the pus-cells entering from the perichondrium, causing absorption of the chondrous substance, and increasing the size of the lacunæ from the periphery toward the center. The destruction of the dense tissues must not be looked upon as the result of the activity of leukocytes alone, for although the phagocytes of all kinds have solvent powers, it is not improbable that the absorption of the osseous and chondrous tissues depends in part upon the activity of the bone and cartilage cells, which are stimulated to unusual action by the inflammatory irritation, and proceed to operate with abnormal energy, multiply, and destroy the perfect tissue in order to accommodate their increased size and number.

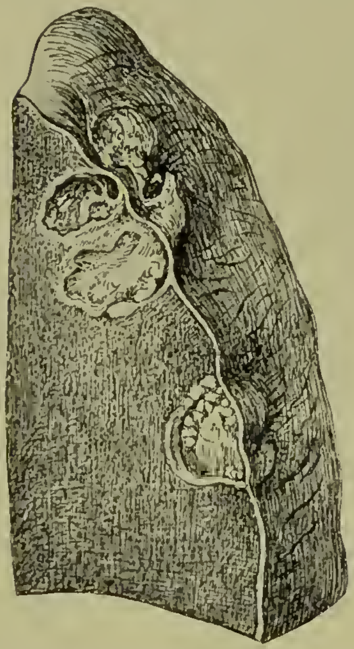

FIG. 206.—Embolic abscesses of the lung (Orth).

An abscess always causes the destruction of the tissue in which it forms, because—

1. The cells of a tissue are sufficient to utilize all the nourishment brought to it, without leaving anything as a food-supply for the leukocytic invaders. If, therefore, large numbers of leukocytes migrate into it and absorb nourishment from its juices, the proper tissue-cells are starved.

2. The inflammatory cells occupy space at the expense of the tissue, whose normal cellular elements are pressed upon and crowded out of existence.

3. The leukocytes penetrate every interstice of the tissue, separating all its component cells and fibers, and in reality disintegrating it.

4. The liquor puris has a macerating and a digesting effect upon the tissues from the presence of proteolytic enzymes.

5. The inflammatory process causing the formation of the abscess stimulates the cells of the tissue to unusual energy, by which, as has already been pointed out, osseous, chondrous, and other dense substances may be absorbed.

Terminations of Inflammation.—The facility with which inflammation recovers will depend upon its severity and the extent of damage done.

Resolution.—The mildest forms of inflammation are said to terminate by resolution, which means that the liquid transudate is conveyed once more to the circulation through the lymphatics, and the leukocytes, after having performed their scavenging function, likewise return to the lymphatics and thence possibly to the circulation. The tissue is thus restored *ad integrum.*

Suppuration.—This has already been described under the formation of abscess. The inflammatory process being too destructive to permit of resolution, the outcome of the process is the formation of an abscess.

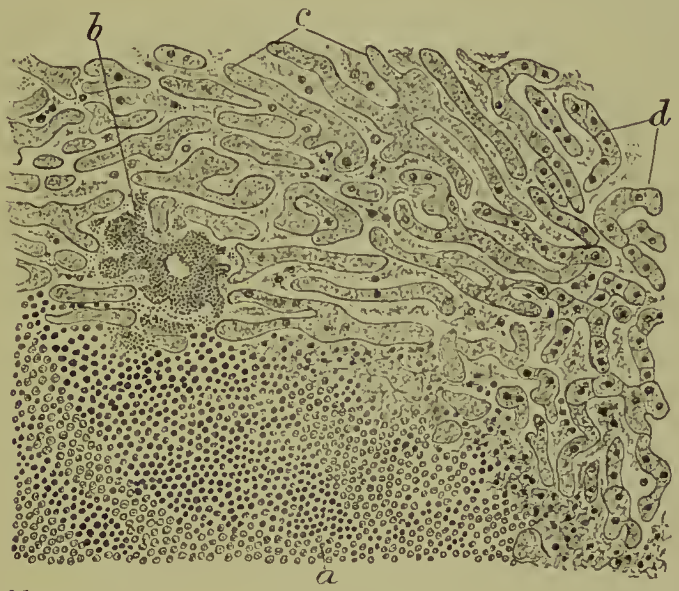

FIG. 207.—Metastatic abscess of the liver: *a*, Dense aggregation of pus-cells; *b*, capillary embolus consisting of micrococci; *c*, necrotic liver-cells; *d*, normal liver-cells (Weichselbaum).

The ultimate tendency of every abscess is to evacuate itself by spontaneous rupture. It must be remembered that the tissues of the body are ever found in a condition of vital tone, in which every portion receives a slight pressure from every surrounding portion. An accumulation of pus in a tissue, occupying increased space, must subject it to an increased pressure from the surrounding tissues, the result of which is to cause the forming pus to extend in the direction of least resistance, until some locality was reached in which pressure was no longer felt.

Such movement of an abscess is technically called "*burrowing.*" The abscess prepares the way for its own movement by macerating, digesting, degenerating, and disorganizing the tissue against which it impinges. Rupture may take place at the surface of the body or into one of its cavities. The latter is less favorable, and may indeed be fatal, by occasioning peritonitis, etc. Rupture may also occur into the circulatory, respiratory, or urinary system, etc., with varying results. Certain abscesses burrow long distances before they are able to evacuate. Thus, the necrotic pus formed in the dorsal spinal region in Pott's disease ("cold abscesses") may burrow to the popliteal space before "pointing." When an abscess finally comes to the surface to rupture, it causes some swelling and is said to "*point.*"

Evacuation may occur spontaneously, the pus escaping with a gush. The evacuation of an abscess leaves a more or less ragged cavity, which partakes of the nature of an ulcer. For a considerable time after evacuation it continues to discharge some pus, a fact which led the older pathologists to believe that a "pyogenic membrane" lined the abscess cavity. What was formerly called the pyogenic membrane is, however, nothing but the peripheral portion of the abscess, in which the tissue, not having completely liquefied and disintegrated, permits the gradual exudation of the pus-cells it contained. When the position of an abscess is such that it cannot rupture, the contents become inspissated and calcify.

Suppurations of certain parts of the body receive special names. Thus, a collection of pus in a serous cavity is an *empyema*, although the term is usually restricted to the pleural cavity and joints. Pus in the pericardium is called *pyopericardium;* in the anterior chamber of the eye, *hypopyon;* in the Fallopian tube, *pyosalpinx;* in the pelvis of the kidney, *pyonephrosis.* Suppurations of the subcutaneous tissue according to the location and appearances are described as *furuncles* or *boils*, *carbuncles*, *whitlows* or *felons*, and *cellulitis.* A suppuration that occurs in the cellular tissue of the neck is called Ludwig's angina, or *angina Ludovici.*

Organization, Cicatrization, or Repair.—This is sometimes spoken of as the conversion of the inflammatory exudate into fibroconnective tissue. There is, however, no reason to believe that the pus-cells whose origin we have found to be the polymorphonuclear leukocytes of the blood possess the power of forming tissue. Their function seems to be exclusively that of scavengers, whose only purpose in leaving the blood vessels is to dispose of the cause of irritation. We must, therefore, consider the formation of connective tissue which characterizes organization as depending upon an activity in the cells of the connective tissue, which, after the acme of the inflammation has passed, are sufficiently stimulated to multiply and develop. Organization may take place independently of suppuration where mild irritation persists, or it may succeed it. In either case the stimulation of the cells is probably mild, though prolonged.

Organization is a most important biologic phenomenon, being the universal process of repair. If we could watch the cells of connective tissue in process of fiber formation, we would doubtless find the primitive round or oval cells, and perhaps the endothelial cells also, becoming transformed into spindle-shaped cells, epithelioid cells, or *fibroblasts*, which, through further changes in the cytoplasm, eventually form fibers. The process, therefore, is analogous to the formation of fibroconnective tissue in the embryo. It is not known how the fibers are formed. It is thought by some to take place through longitudinal cleavage of the cells; by others, through exudation from the cells. A peculiarity of the new connective tissue that the student should never forget is its *marked tendency to contract*, a benign tendency when the edges of healing wounds are to be drawn together, but a most pernicious one when thickened bands of tissue penetrating organs of the body press upon their functional elements and cause them to atrophy.

The irregular openings remaining in the tissue after abscess evacuation has been completed must in some way be repaired. The walls of the abscess gradually become freed from the invading leukocytes, and the necrotic tissue forming the so-called pyogenic membrane gradually becomes covered with groups of growing cells, familiar to every surgeon as *granulation tissue.* Granulation tissue is composed of *granulations*, or groups of growing cells surrounding vascular loops. These growing cells surround sprouts from pre-existing capillary blood vessels, and are actively engaged in forming new connective tissue between the cavity originally occupied by the pus and the surrounding, no longer inflamed, tissue. As soon as the pus has been discharged, the cavity of the abscess collapses because of the normal pressure of the surrounding tissue. When the surfaces covered with growing cells come in contact, union by fusion takes place, and the cavity is gradually obliterated. In this way what may have originally appeared as an enormous gap in the tissue is eventually transformed either into a node or a cord of fibroconnective tissue, in which it is difficult to find the slightest trace of the original condition.

In the organization following suppuration no other tissue than fibroconnective tissue is formed, and it is only at a later period, if at all, that any restitution of the original muscular, nervous, glandular, or other tissue of the organ takes place.

Two kinds of granulation tissue are described: the *fibroid*, which is that usually seen and already described, and which leads to the formation of connective tissue, and the *adenoid*, which is so called from the resemblance it bears to the structure of the lymphatic glands. It consists of a more or less well-developed fibrous reticulum, whose meshes are filled with lymphocytes and fibroblasts. Its formation indicates that the irritation is not yet overcome, and the development of fibroconnective tissue is being retarded. Tissue of this kind is seen in tuberculous lesions, especially in such loose tissues as the subperitoneal areolar tissue.

The surface of every ulcer is covered with granulations, forming granulation tissue. The degree of natural stimulation which these receive from contact with the air, the crusts which form upon them, and from foreign bodies, etc., is usually sufficient to enable the tissue to grow properly and effect a prompt healing. If, however, through deficient nutrition or other cause, the granulation tissue ceases to grow, the ulcer becomes *indolent* and healing is retarded until some artificial stimulus, such as an application of lunar caustic, is made. On the other hand, the accidental infection of granulation tissue sometimes causes multiplication of cells entirely out of proportion to the necessary fiber formation, and the granulations grow large and prominent, and form *exuberant granulations*, or "*proud flesh*," which retard further repair unless removed by the knife or scissors or burned off with caustic applications.

When the inflamed tissue is a serous membrane, the organization is commonly *plastic*, and leads to the formation of what are known as *adhesions*, which usually form where the denuded surfaces of the inflamed membranes have been agglutinated by sticky fibrin. The inflammation and fibrin formation, or fibrinoid degeneration, have been followed by the destruction or displacement of the covering endothelium, so that the surfaces in contact are denuded and well calculated to grow together. From the subendothelial layers, through the still persisting fibrin framework, the fibroblasts grow and form fibers binding the two membranes together, so that a firm fibrous union finally occurs. As the inflammatory process finally disappears and movement is again possible, the adhesions limit it according to their extent. If movement is still possible in spite of the adhesions, the new connective tissue is subjected to more or less constant tugging, and the adhesions gradually attenuate until they are transformed into fibrous cords connecting the no longer closely approximated surfaces. This process is common to the peritoneal, pleural, pericardial, meningeal, and other serous membranes.

Histology of Acute Inflammatory Lesions.—The hyperemia and edema which begin the inflammatory process cannot with certainty be differentiated from more simple processes, hence the only microscopic criterion for the recognition of inflammation is the presence of inflammatory cells in the tissue. The source of the greater number of these has already been traced, but as the transmigrated leukocytes are not the only important cells which appear in inflamed tissues, it seems well to speak of the different cells in detail.

1. **The Leukocytes.**—The chief cells in point of numbers are the *polymorphonuclear leukocytes*, which transmigrate from the blood vessels. As these cells pass through the vessel-walls, they usually collect more or less plentifully immediately outside the vessels, where they at first form clusters, then penetrate into the deeper tissue to the actual focus of irritation. The cells do not seem to change their appearance in any way, but present all the characteristics by which they are recognized in the blood.

Lymphocytes, both large and small, also appear in inflamed tissue, the large lymphocytes or hyaline cells predominating in numbers. Small lymphocytes, having no visible cytoplasm, cannot be phagocytic, but the large lymphocytes are actively phagocytic and are regarded by many writers as among the most important scavenger cells. *Eosinophilic cells* may or may not be present. It is usually observed that if the serous membranes are inflamed, the eosinophilic cells usually predominate in numbers in the early stages, later being replaced by the polymorphonuclear cells.

In very mild degrees of inflammation the large lymphocytes may be the only cells to appear. In the section upon Diseases of the Blood (*q. v.*) the peculiarities of the different leukocytes and the methods of differentiating them will be found in detail.

The recognition of the polymorphonuclear leukocyte, the eosinophile, and the small lymphocyte is easy, but quite a different problem confronts us when we attempt to decide with certainty the histogenesis of the cells which are included under the term large lymphocyte While there can be little doubt but that the large lymphocyte of the blood appears in inflamed tissue, there are other cells of *celomic* origin that may readily be confounded with it. These latter cells are large in size, possess cytoplasm free of granules, and a single vesicular nucleus which stains palely. It is supposed that many of these are derived from the fixed, and perhaps some from the wandering, connective-tissue cells. Their phagocytic activity proclaims them of importance in combating the source of irritation, though they may have for their chief function the post-inflammatory connective-tissue regeneration. The difficulty of distinguishing between such hyaline cells of vascular and of celomic origin has probably been the cause of the once wide-spread error that connective-tissue formation depended upon the activity of leukocytes.

The relative proportion of these different cells seems to depend upon the nature of the process. Thus, when the inflammation is mild, the hyaline cells seem to be particularly numerous, while when the inflammatory process is active, the polymorphonuclear cells more and more outweigh them in numbers, until, when pus is finally formed, few other cells are observed. Just what causes determine which cells shall predominate and through what influence the different cellular invasion is governed is unknown. It may be some chemic variation in the inflammatory products, as we find that peculiar inflammatory conditions, such as are excited by the presence of certain parasites, notably trichina, greatly augment the number of eosinophiles that appear.

2. **The Plasma Cell.**—There is considerable confusion at the present time concerning plasma cells, because different authors have applied this name to very different elements. The plasma cell of Unna is apparently identical with the "Mastzelle" of Ehrlich, and will be described as such. The plasma cell, as it is recognized by most writers of the present time, is probably of hemal origin. It is not known from what leukocyte or by what process it is formed. It is usually observed in greatest numbers in acutely toxic conditions, and is, therefore, most abundant in the lesions of diphtheria and other toxic diseases. The cells are usually a little larger than leukocytes, of ovoid shape, have a hyaline cytoplasm which absorbs the nuclear stain slightly, and a nucleus of vesicular character, rich in chromatin, which is almost invariably placed excentrically in the cell. Such cells are found in nearly all inflammatory lesions, but their purpose is unknown.

3. **The "Mastzelle,"** or musting cell, the plasma cell of Unna, was carefully studied by Ehrlich. It is larger than any of the cells thus far described, may be regular or irregular in outline, and is, therefore, probably ameboid, has an oval vesicular nucleus, but is chiefly characterized by an extremely granular cytoplasm. The granules are very fine, and have a strong affinity for basic dyes. They stain well with hematoxylin. "Mast-zellen" are not always present in inflammation, appearing to be most frequent in inflammation of the mucous membranes. The nature of the granules is not determined, and the significance of the cell is unknown. As this cell not infrequently presents itself in the neighborhood of tumors, especially when they contain mucin, as it sometimes appears in what may, with reason, be regarded as normal submucous tissues; and as it rarely appears in great numbers in inflammatory accumulations, it may with propriety be questioned whether it is an "inflammatory cell."

4. **The epithelioid cell** is a large oval or elongate cell with hyalin cytoplasm and an oval vesicular nucleus which contains but little chromatin. It is very probable that this cell is derived from the fixed cells of the connective tissue, and probably also from endothelium. It is usually found in mild inflammatory processes or at the termination of acute destructive

processes, and is the probable antecedent of the *fibroblast* or connective-tissue builder. Viewing the histogenesis of the cells from this standpoint, it seems correct to speak of the younger, more oval, cell as the epithelioid cell, the older, more distinctly elongate, cell as the fibroblast.

Fibroblasts are large cells of distinctly spindle shape, with ovoid or rod-shaped nuclei, poor in chromatin. They appear only in the stage of repair, and are extremely numerous in cicatricial tissue. Their resemblance to the fibroblasts of the embryo and the circumstances under which they make their appearance leave little doubt as to their office.

5. **Giant-cells** make their appearance in many inflammatory processes, and originate in different ways. Marchand introduced bits of hair into the cornea and other tissues, and found them surrounded by giant-cells evidently formed by the fusion of cells, possibly leukocytes.

It is a common observation that in wounds containing bits of foreign substance too large to be incorporated by phagocytes, giant-cells are of frequent occurrence, and it seems reasonable to infer that when a foreign body is too large to be attacked successfully by a single phagocyte, neighboring cells coalesce in order to combine their efforts at its solution and removal. The cells may also be formed by multiplication of nuclei without division of the cytoplasm. These giant-cells are active, vital, and functional, and thus differ altogether from the giant-cells found in tuberculous and sarcomatous tissue.

Their size varies, probably according to the conditions of their formation, and they contain from two or three to a dozen nuclei, but never attain a size approaching the giant-cells of tubercle.

Interpretation of the Phenomena of Inflammation.—A careful analysis of the phenomena of inflammation leads us to the broad generalization that they are conservative in tendency, benign in disposition, and evidently the result of a carefully adjusted protective mechanism.

The inflammatory hyperemia, with its associated edema, exerts a diluting and solvent action upon the irritant, and tends to remove and scatter it, thus lessening its injurious effects. The cellular infiltration of the tissue is succeeded by phagocytosis, with probable destruction of microparasites and solution of irritating particles. Failing by these means to dispose of the source of irritation, the further invasion of inflammatory cells, with the suppuration, colliquation, burrowing, and pointing, is but a preliminary to its final ejection as the abscess evacuates. The phenomena of cicatrization are but the final reparatory processes.

When an irritation is mild and continuous in action, the phenomena attending it are different from those described, and characterize the condition known as *chronic inflammation.*

Chronic inflammation results from continued irritation.

Etiology.—It may follow acute inflammation, or may be chronic from its very inception if it depends upon the continuous or repeated irritation of certain substances in the circulating blood, as alcohol to the liver and lead to the kidneys. It, therefore, may be either toxic or infectious.

Pathology.—It is essentially different from acute inflammation, and except that it is a reaction of irritation and itself a reactive process, should not be described as inflammatory.

Chronic inflammation is chiefly characterized by *fibrosis*, or new fibroconnective-tissue formation. All the essential phenomena of acute inflammation—hyperemia, edema, cellular infiltration, colliquation, and suppuration—are absent, and the condition is characterized instead by slow and progressive hyperplasia of connective tissue, months, or perhaps even years, being required before it becomes sufficiently important to make itself symptomatically obvious.

The proliferated connective tissue occurs as exaggerations of the fibrous framework of organs or as cicatricial masses in the cellular tissues. It is formed by multiplication of the connective-tissue cells and the formation of new fibers. Only occasionally does one find the tissue occupied by isolated leukocytes or other inflammatory cells.

Morbid Anatomy.—The new formation of connective tissue is a menace to the health of the part in which it occurs. The fibrous tissue, by pressure upon the proper parenchyma of the organ, causes atrophy, which, combined with the contraction of newly formed connective tissue, transforms the diseased organ to a small indurated mass.

The fibrosis and atrophy rarely progress uniformly, so that the surface of the affected organs is usually irregular and marked by furrows, pits, and depressions, resulting in part from atrophic loss of substance, in part from contraction of the newly formed connective tissue. The most interesting example of this is found in cirrhosis of the liver, where the irregularities upon the surface are so striking as to give the organ the name "hob-nail liver," and in chronic interstitial nephritis, where the once smooth surface of the kidney becomes coarsely granular.

Pathologic Histology.—So closely does the newly formed connective tissue resemble the normal that it may be impossible to differentiate between them, and it may be only by noting the relative proportion of fibrous tissue that its increase can be determined.

Fibrosis is a wide-spread process affecting the valves of the heart and its lining membrane in chronic endocarditis, the aorta and blood vessels in arteriosclerosis, the major organs in cirrhotic hepatitis, interstitial nephritis, atrophic gastritis, etc., yet it is nearly always referable to local or systemic intoxications, among which alcoholism, syphilis, lead-poisoning, gout, and rheumatism are most important. Even the fibrosis of senility may be referable to inadequate action of the kidney or of some other organ by which irritating substances are retained in the blood. It seems improbable that any single irritant can be present in the blood in all the varying conditions. Much more probably any substance sufficiently stimulating to hasten cellular activity may induce it.

The Healing of Wounds.—The older writers upon surgery were accustomed to describe five methods by which wounds healed: (1) Immediate union; (2) first intention; (3) second intention; (4) secondary adhesion; (5) beneath a scab. Immediate union, which signified the actual union of cell to cell, fiber to fiber, etc., is now known to be impossible, and it is recognized that healing under a scab does not differ in any essential from other modes of healing. We need, therefore, only consider—

1. Healing by first intention.
2. Healing by second intention.

These modes of healing are identical so far as the process itself is concerned, but vary slightly according to local conditions.

In every wound the surface epithelium is divided, the deeper tissues separated from one another, and the blood vessels opened. The immediate effects are gaping of the wound and hemorrhage. After the natural causes, described in the section upon hemorrhage, have checked the flow of blood, the wound remains filled with blood, which coagulates, retracts, and draws and holds the surfaces together. Upon the surface a crust or scab soon forms through the drying of the exuded fluids.

If such a wound is free from infecting bacteria, repair at once begins. The divided tissues are in contact with an abnormal substance—coagulated blood—and are mildly irritated by it, with the result that hyperemia, exudation, transmigration of leukocytes, and proliferation of connective tissue occur. The coagulated blood gradually disintegrates, and the fragments of corpuscles, granules of pigment, and shreds of fibrin are removed by the activity of phagocytes. As the coagulum disappears, the cells of the tissue on each side of it grow and extend into it, so that the clot becomes a kind of scaffolding upon which the new connective tissue is built up. In the course of a day or two new fibers begin to bridge over the interval, and in three or four days the new tissue begins to be fibrous. The tissue formation keeps pace with the absorption of the clot, until, when it has entirely disappeared, the gap is completely filled with embryonal connective tissue. The dry scab upon the surface, no longer being held in place by fibrinous filaments descending into the general coagulum and being impinged upon all sides by the growing cells of the epithelium, drops off, and a smooth glazed surface is left upon which the epithelium rapidly grows from the surrounding tissue. When thus freshly repaired, the wound appears red and the new tissue soft and tender. The subsequent contraction of the connective-tissue fibers, however, reduces its size and causes it to whiten. The size of the remaining cicatrix depends entirely upon the accuracy with which the tissues were approximated before healing set in. In sutured wounds or in wounds whose edges are firmly held in apposition by plaster comparatively little new tissue is formed, and the cicatrix appears as a delicate, pale line. It is this process that is called *healing by first intention*. If, however, the wound were permitted to gape widely, so that considerable new tissue were required to bridge it over, the cicatrix appears correspondingly large and perhaps disfiguring.

In infected wounds the course of events is quite different in that the process of healing is interrupted by the phenomena of suppuration. Chemotactic influences develop, leukocytes appear in the walls of the wound in large numbers, and degeneration, disintegration, colliquation, and suppuration occur, the tissues surrounding the wound melting away before the invading bacteria and cells. When the activity of the micro-organisms is checked by the occurrence of local immunity and the abscess evacuates, a considerable sized space remains, the walls of which are but mildly irritated by the particles of necrotic tissue, the dead bacteria, the exuded leukocytes, etc., that have not yet been removed. This mild irritation, added to that occasioned by the drying effect of the atmosphere upon the wound, and the numerous slight accidental stimuli brought to bear upon it, keep the tissues active, and stimulate new tissue formation by means of which the final healing is brought about. The exposed surface of the wound soon shows granulations in large numbers, and from all parts of the bottom and sides new connective tissue begins to grow. If such a wound, after the cessation of suppuration, can have its surfaces brought into contact without danger of further infection, the repair is much accelerated, but usually the surgeon packs it with gauze, keeps it open, and consequently compels it to heal "from the bottom." This healing from the bottom is what the surgeons describe as *healing by second intention*, or *granulation*. The process is the same as healing by first intention, except for the absence of the scaffolding upon which the formation of new tissue can immediately begin.

The *healing by secondary adhesion*, often mentioned by surgeons, is not a definitely characterized mode of healing.

Sometimes the newly formed connective tissue characterizing the healing of wounds fails to pass through the usual metamorphoses and forms a contracting cicatrix, but continues to grow, the resulting tissue masses being known as keloidal growths or *keloids*, and supposed to be related to neoplasms.

Regeneration of Tissue.—The destructive effects of inflammation and other disease processes are not infrequently succeeded by repair, the perfection of which depends chiefly upon the complexity, vitality, and specialization of the tissues concerned. In the main, repair is accomplished through the formation of new connective tissue, through intermediate granulation tissue. Concomitant with or subsequent to the connective-tissue repair, regenerative changes in other tissue elements may take place.

Epithelial Tissues.—Surface epithelium, whether of the simple pavement form, the simple columnar type, or the transitional pavement or columnar types, regenerates readily through the multiplication of the cells adjacent to the wound. In large superficial ulcerations much time may elapse before the continuous growth from the edges is able to cover the entire surface, and during the interval the growth of micro-organisms upon the denuded surface, as well as other accidents, may interrupt or inhibit its growth.

The remarkable facility for growth possessed by the epithelial cells is well illustrated in *skin grafting*, in which, in order to accelerate the healing, the surgeon removes fragments of the epidermis from healthy portions of the skin and transplants them to the surface of the wound, where they at once begin to grow. By thus increasing the number of centers from which the growth of the cells can take place, the epithelium much more quickly regenerates.

Columnar epithelium, while more delicate than squamous epithelium and probably not susceptible of transplantation, regenerates similarly by multiplication of the remaining cells, as is abundantly illustrated in the healing of typhoid ulcerations of the intestine and peptic ulcerations of the stomach.

The regeneration of the more highly specialized epithelial structures which enter into the composition of organs is a much more complicated matter.

(*a*) *The Mammary Gland.*—It is not certain that destroyed mammary tissue regenerates. In cicatrices resulting from the healing of wounds and the cicatrization of abscess cavities, signs of regeneration of the glandular structure are usually wanting. The ability of the gland to increase its secreting substance, in anticipation of lactation, by the formation of new acini by processes budding from preëxisting ducts and acini, suggests that, should the presence of dense cicatricial tissue or other unfavorable conditions not intervene to prevent it, the mammary gland would readily form new tissue to replace what had been destroyed. The pancreas and salivary glands, having an analogous structure, probably possess similar capabilities.

(*b*) *The Liver.*—It is not known positively that the hepatic tissue regenerates. Being a tubular gland, it is conceivable that new secretory structures may be formed by budding offshoots from the remaining structure. What seems to be an attempt at this is observed in cirrhosis and other destructive diseases with atrophy, in which a marked and remarkable proliferation of small bile-ducts takes place. There seems to be no particular reason for the existence of these ducts; their appearance is quite atypical, and their presence is now generally interpreted to signify an attempt at the formation of new secreting substance by offshoots from the ducts.

(*c*) *The Kidney.*—That whole uriniferous tubules regenerate, and that new glomerular capillary tufts can form to connect with them, is very improbable. Indeed, it is uncertain whether the kidney regenerates further than to repair its injured and desquamated epithelial cells. This seems to be readily accomplished, as cases of acute nephritis with desquamation of the cells recover completely. Remembering that the kidney has a double function—that of removing water from the blood through the glomerular tufts, and of secreting important solids by its glandular cells, we can conceive the possibility of any regenerative efforts being directed toward the compensation of the simpler of the two functions. If, therefore, the normal tubules were to give off tubular branches containing secretory cells, the secretory function of the organ might be assisted even though the water elimination might not be provided for.

Muscular Tissues.—The *unstriped muscular tissue* seems capable of regeneration by multiplication of its cells. Its ability to do so is limited, however, as we find in the repair of wounds and ulcerations of the stomach and intestine that the newly formed tissue is almost purely fibrous.

The *cardiac muscle* also seems to have a very limited ability to repair damage. Acute suppurative myocarditis with loss of muscular substance and embolism with resulting focal cardiomalacia are nearly always followed by the formation of fibroid patches in the wall of the heart, without new formation of fibers.

The *striated muscular tissue* regenerates to a limited extent, the regeneration taking place solely through activities in the living tissue. In about two days after a muscle is injured it is found that at the ends of the injured or lacerated fibers a multiplication of the muscle-cells takes place, both in the still attached and living fibers and in the separated fragments.

In the ends of the attached fibers this multiplication of cells forms nucleated sarcoplasmic masses resembling giant-cells. These, which are sometimes called buds, gradually grow into the cicatrix, thus increasing the length of the fiber. The development of striations and the formation of fibrilla do not occur until later. As the buds extend into the tissue, they frequently split up into several portions, thus appearing to increase the number of fibers, though they are smaller than normal.

The cells that grow in the isolated muscle fragments rarely attain much importance. They first appear like large epithelioid cells, but later the multiplication of nuclei transforms them to giant-cells much like those seen on the ends of the growing fibers. It seems probable that these masses, not being associated with the muscle substance, mostly die, although they can be found in cicatrices a month or two old. Should they be able to progress to perfection, it is probable that the successive steps would resemble those seen in the budding fibers—viz., the development of cross-striations and later fibrillation.

The chief regeneration after muscle injuries is always in the connective tissues, by which only cicatricial and not muscular tissue is formed. Although the amount of newly formed muscular tissue is sufficient to show that the tissue regenerates somewhat, enough new muscular tissue is never formed to be of much importance. In order that muscle regeneration can occur, it is essential that the tissue be well nourished, though it is not essential that it receive nervous impulses, as once supposed.

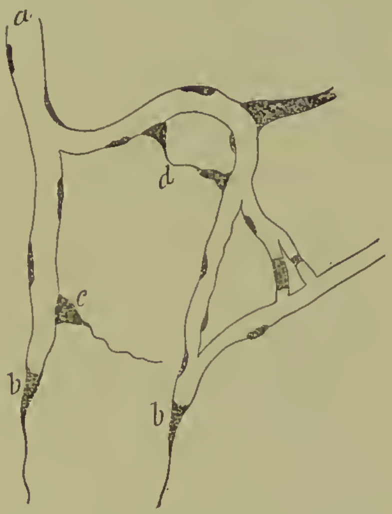

FIG. 208.—Formation of new blood vessels, as seen in the tail of a tadpole: *a*, Capillary vessel extending by means of a terminal protoplasmic filament (*b*); *c* and *d*, protoplasmic filaments or offshoots by which a capillary reticulum will eventually be formed (Arnold).

Blood Vessels.—The new blood vessels so conspicuous in granulation tissue and forming an essential element in the development of the cicatrix are derived, by budding, from preëxisting vessels. The careful investigations of Arnold have shown that from the wall of a capillary blood vessel a conic outgrowth makes its appearance, rapidly elongates, and terminates in a delicate filament. Many such filaments make their appearance simultaneously in tissues in which rapid vascular formation is taking place. The filaments extend into the growing cellular mass until they meet similar filaments from other conic processes. Having united, they form a solid protoplasmic cord connecting the capillaries. Excavation of this cord begins at both ends, the circulating corpuscles impinging little by little upon the excavation, which becomes deeper and deeper until a distinct channel extends into it for a considerable distance at each end. Ultimately the canalization reaches the center and a new capillary is formed.

In pathologic processes, such as neoplasms, hyperplasias, chronic inflammatory and hyperemic conditions, the new vessels of large size make their appearance, by primary capillary formation, with secondary formation of the adventitia and media by a gradual downward growth from the muscular and fibrous tissues of the larger vessels.

The newly formed blood vessels in regeneration may be permanent, but are usually formed solely for maintaining the nutrition of the temporary granulation tissue, their function terminating with the cicatrization of the wound, after which they disappear, this disappearance depending upon the contraction that takes place in the cicatricial tissue.

Every one who has had experience with wounds knows that a fresh scar is red from the presence of capillary blood vessels, but that an old scar becomes white, the blood vessels having disappeared.

Cartilage does not regenerate. Wounds of cartilage are repaired through the formation of fibroconnective tissue only.

Osseous tissue undergoes as perfect a regeneration as any tissue of the body through the calcification and subsequent ossification of an embryonal tissue known as *callus*. (See Diseases of the Bones.)

The **nervous tissues** regenerate or fail to do so according to their specialization. The ganglionic nervous tissue, being of very high specialization and consequently of low vitality, fails to regenerate when destroyed. The consequences of this failure are familiar in such lesions of the nervous system as poliomyelitis, bulbar palsy, etc., in which the ganglionic cells, being destroyed, and failing to regenerate, permanently interrupt the function of the associated muscles.

The destruction of the ganglion-cells is followed by degeneration of the nerve-fibers. The toxic degeneration of the peripheral nerves and the traumatic lesions of the nerve-fibers may, however, repair.

Unfortunately, there are many particulars concerning the regeneration of nerve-fibers upon which information is lacking. When a nerve-fiber is severed, the proximal fragment usually degenerates to the node of Ranvier, next above the section, while the distal fragment undergoes complete degeneration.

About two days after the injury, and after signs of irritation from local causes have disappeared, the central end of the nerve begins to grow. In amputations in which there is no distal end, the growth of the central end causes the gradual formation of a mass of embryonal tissue consisting of spindle cells, derived from the endoneurium, and fibers grown from the axis-cylinders. When these masses become large enough to be noticeable, they form tumors known as *amputation neuromata*.

If the limb has not been amputated, the new outgrowths from the axis-cylinders of the central end of the nerve begin to grow down in the path of the medullary sheaths, extend through whatever cicatricial tissue may be at the seat of injury, and on into the distal portion. The remaining steps are variously described by different authors. Ziegler and Stroebe observed the new nerve-fibers most perfect when they were able to grow into the sheaths of the old nerves. They found the distal fragment completely degenerated. The regeneration of the nerve, therefore, occurred solely through the continuous downward growth of the central fragment.

Other observers find that only a part of the distal fragment degenerates, and that continuity is established by the successful downward growth of the central fragment and its union with the remaining vital distal fibers. Still others think they see signs of regeneration in the peripheral fragment, which, as the axis-cylinder degenerates, shows a proliferation of the cells of the nerve-sheaths and the presence of certain phagocytic cells which take up the myelin droplets set free. They think that it is through the agency of these proliferated cells of the sheath that the new axis-cylinders are formed. The weight of evidence seems to be in favor of the opinion of Stroebe and Ziegler that the new axis-cylinder is formed, not by the proliferated cells of the sheath, but by the new growth from the proximal fragment. It seems probable, however, that the multiplication of the cells of the sheath exerts a nutritional influence upon the growing axis-cylinder. It is supposed that the regenerating axis-cylinders occupy the sheaths of the old fibers, because they afford the direction of least resistance. This can scarcely be accepted, however, and it seems more likely that they follow some attractive influence or neurotropism.

The tendency to grow in the old sheaths has lent some support to the view that the new fibers are formed within the old sheaths by the multiplied cells, and not by downward growth from the proximal fibers.

Regenerative attempts have been described in the spinal cord, where, in complete breach of nervous conduction, such as is seen in transverse myelitis and the growth of tumors, presumably regenerating nerve-fibers seem to grow out into the spinal membranes, descend past the seat of disease, and reënter the cord below it.

INFECTIOUS DISEASES CHARACTERIZED ESSENTIALLY BY LOCAL MANIFESTATIONS OF SUBACUTE OR CHRONIC FORM.

THE SPECIFIC GRANULOMATA.

In addition to the inflammatory conditions which have been described, and which, inasmuch as they do not depend upon any single micro-organism, cannot be called specific, there are a number of diseases, characterized essentially by inflammatory phenomena, which depend upon micro-organisms unknown except in the particular diseases in which they occur, and provocative of those diseases when artificially inoculated into animals. These are the *specific inflammations*. In nearly all of them the lesions are focal, and the course subacute or chronic, resulting in circumscribed collections of granulation tissue which, upon first sight, resemble neoplasms, and have caused them to be called "*specific granulomata*."

Although each disease has characteristics by which it can usually be recognized without difficulty, the lesions found in each disease are by no means uniform, varying according to the rapidity of formation, the virulence of the micro-organism, the associated micro-organisms, and the susceptibility of the individual.

TUBERCULOSIS.

Tuberculosis is a specific, infectious, inflammatory disease of man and the lower animals, caused by the Bacillus tuberculosis, and characterized by a subacute or chronic course and the formation of more or less circumscribed nodules, known as tubercles.

A tubercle, the characteristic lesion of the disease, is an inflammatory and degenerative nodule formed about one or more tubercle bacilli.

The disease commonly called "consumption" or "phthisis" in its pulmonary form is one of the most wide-spread and fatal maladies, being found among all peoples and in all countries. According to statistics collected by Schmaus, *one-seventh* of mankind die of tuberculosis, while in the bodies of those who die of other causes tuberculous lesions are present in from 40 to 50 per cent. About 30 per cent. of infants die of tuberculosis, and its lesions are present in 18.8 per cent. of those dying of other causes.

Tuberculosis also occurs among the lower animals. It is common among cattle, and has been observed in many other mammals, notably monkeys, hogs, rabbits, guinea-pigs, sheep, dogs, horses, cats, and lions. It also occurs in birds, especially in parrots, and a few cases have been recorded in reptiles and batrachians.

Among men the disease is wide-spread, affecting all ages, both sexes, all social conditions, in all climates. It is almost never hereditary or congenital, though the offspring of those suffering from tuberculosis seem to inherit some physical weakness or constitutional taint making them more predisposed to it than others. For the same reason all hygienic errors, such as overwork, overcrowding, bad food, bad ventilation, frequent pregnancy and prolonged lactation, residence in damp atmospheres, exposure to cold and wet, and mental worry and exhaustion predispose to it. Damp and unequal climates also favor tuberculosis.

Etiology.—Tuberculosis is caused by the Bacillus tuberculosis, which was discovered by Koch in 1882. While minute inflammatory nodules, somewhat resembling tubercles, may be caused by other bacteria and by minute irritating particles, such as powdered glass, etc., the true tubercle is caused only by this organism.

The original source of infection is unknown, and the bacillus is now known to us only as a parasite, found in the diseased tissues and discharges of tuberculous animals.

Probably the chief sources of infection have to do with *air* and *food*, through which means the exciting bacteria find their way into the body.

The *air* becomes a distinct menace to both the predisposed and normal individual when it contains tubercle bacilli in the dust or in finely pulverized pulmonary secretions thrown out by consumptives in the act of coughing. Bacilli occur in the air only where it is contaminated by infected individuals. Rooms and workshops frequented by them are particularly dangerous. The same fact holds good for cattle, who readily become diseased when stabled in close quarters together with diseased animals.

Foods are dangerous only when containing tubercle bacilli in the living state. The milk and flesh of tuberculous cattle are, for this reason, rejected in all well-regulated communities. The flesh which is sterilized by cooking is, however, more rarely a source of infection than the milk which is consumed raw.

Tuberculosis, while eminently infectious, is only slightly contagious. The chief danger in associating with sufferers from the disease is the inhalation or ingestion of the bacilli accidentally discharged into the air during coughing or deposited upon napkins, handkerchiefs, and towels.

Fomites, no doubt, play a considerable part in the spread of the infection, as in a variety of ways that will suggest themselves to the reader the patient may most innocently deposit bacilli upon articles handled.

The tuberculous infection may take place by any of the usual routes, although the infrequency of tuberculosis of the genital organs and the rarity of the bacillus in wound infections show us that these are rare avenues. The bacilli operate locally, and even when, by accident, admitted to the circulation, do not remain in the circulating blood, but lodge in the capillary vessels. They almost never pass through the placenta to infect the unborn offspring.

The principal routes of infection are, therefore, the respiratory and digestive apparatus, with the balance greatly in favor of the former, as it seems evident that in the natural order of things bacilli suspended in the atmosphere should more readily enter the lungs than the alimentary canal. However, bacilli inhaled may, by falling upon the pharyngeal mucous membrane, be swallowed. The lung is the organ most commonly infected in cases of human and bovine tuberculosis, which adds additional confirmation to the suspicion that the infection results directly from the inhalation of the bacilli, though swallowed bacilli may be taken up through the lacteals, thrown into the veins, and so carried to the lungs.

In experimental tuberculosis it is found that the lung is not usually infected in the manner suggested, but that the tonsils, the intestine, the mesenteric and retroperitoneal lymphatic nodes, the liver, and the spleen show the lesions. This seems to indicate that pulmonary tuberculosis more likely depends upon inhalation than upon ingestion of the bacilli. However, the lesions do not always develop first in those organs into which the bacilli are first received. From both intestine and lung bacilli may be absorbed into the circulating blood and carried to remote parts of the body; otherwise it would be difficult to explain the not infrequent cases of primary tuberculosis of the brain, bones, joints, liver, kidney, etc.

While, therefore, it is certainly true that many cases of tuberculous infection take place through the intestine, and appear first in the lung and in other organs, it is most reasonable to believe that the majority of pulmonary infections are direct.

The nature of the constitutional peculiarity characterizing *predisposition* is unknown.

Bacteriology.—The disease is caused by the tubercle bacillus of Koch.

Morphology.—The tubercle bacillus is a delicate elongate organism measuring 1.5 to 3.5 x 0.2 to 0.5 μ, having rounded ends, usually occurring singly, never in chains. Small groups of them commonly have a parallel, slightly overlapping arrangement resulting from their mode of growth. Branched forms are not infrequent. The cytoplasm is more or less homogeneous in young organisms, although in old bacilli, especially such as are observed in tuberculous sputum and pus, it is fragmented so that the organisms present alternating colored and colorless areas which give them a beaded appearance. It is supposed that the spaces in the beaded bacilli are intervals between fractured and probably degenerated protoplasm. Rarely each or many of the bacilli found in a sample of sputum contain large granules—chromatophilic granules—of rounded form, and of a diameter greater than the bacillus itself. The significance of these is unknown.

The organism is not motile, has no flagella, and forms no spores.

Staining.—The bacillus stains with difficulty. The ordinary aqueous solutions used for staining bacteria make very little impression upon it, and to color it satisfactorily a stain containing a mordant—Ziehl's carbol-fuchsin, Ehrlich's anilin-water gentian-violet, etc.—is required. It stains well by Gram's method.

The tubercle bacillus is one of a group of organisms called "acid-proof," because the substance is with difficulty penetrated by mineral acids. This peculiarity, discovered by Koch, is made the foundation of the differential methods of staining. Probably the most generally useful method is that in which cover-glasses spread with sputum, or sections of tissue, are first immersed for some minutes in warm carbol-fuchsin, and then carefully and thoroughly washed with a 3 per cent. solution of hydrochloric acid in 70 per cent. alcohol.

Cultivation.—The cultivation of the tubercle bacillus is difficult. The organism is started with difficulty, and will grow only in a highly concentrated medium. Koch first isolated it upon bovine blood serum. Roux and others found glycerin-agar easier to handle and quite as useful. Theobald Smith found dog's blood serum to be the best medium. From the lesions selected as most appropriate for the purpose a small fragment is removed with sterile instruments under conditions of absolute asepsis, and laid upon the surface of coagulated dog's serum in a test-tube. After some days' sojourn in the incubating oven at 37° C. this bit of tissue, in which the bacilli have been growing in the mean time, is spread over the surface of the serum, and the bacilli thus distributed again kept at 37° C. for growth. If thus successfully isolated, the bacilli can usually be subsequently grown upon blood serum, glycerin-agar, glycerin bouillon, and glycerinized potatoes.

The growth of the bacillus takes place only in the presence of uncombined oxygen.

The general appearance of the growth is the same whatever the medium upon which it grows. It forms a grayish-yellow or cream-colored, moderately dry, dull, wrinkled, spreading mass, which heaps up in the central older parts of the culture and thins at the edges. The appearance is usually sufficiently characteristic to enable a diagnosis to be made of the culture by simple inspection, though the cultures vary, some lacking the dull, wrinkled appearance.

Chemistry.—Cultures of the tubercle bacillus give off a peculiar heavy, sweet odor. The reaction of the culture medium is not changed. No change visible to the naked eye is produced in any of the media upon which the bacillus has grown. No enzymes are produced; gelatin is not liquefied nor milk coagulated.

From the cultures, by extraction, condensation, and filtration, a peculiar substance known as *tuberculin* is secured. It is not the active toxic principle, although it causes a febrile reaction when injected into tuberculous animals, and can be used as a diagnostic agent.

The composition of the tubercle bacillus has been carefully studied by de Schweinitz, Levene, and others. Its irritative property seems to reside, at least in part, in an irritating fatty substance which it contains. It is probably either this same fatty substance or a peculiar waxy substance also present that prevents the decolorizing action of the mineral acids applied to stained preparations.

Pathogenesis.—All cultures of the tubercle bacillus are not pathogenic, nor is any culture pathogenic for all animals. This difference has led to the creation of special varieties of the tubercle bacillus, the important ones being the *human*, *bovine*, and *avian*. Whether these have originally been identical, or may even yet be identical, is not decided. It seems as if the evidence of any other difference existing than can be explained by the different conditions under which the organism grows in different animals is very slight.

Lesions.—The lesions produced by the tubercle bacillus vary according to the number of bacilli introduced into the animal, the mode of introduction, and the variety and susceptibility of the animal.

Koch found that when large numbers of bacilli, such as are contained in a suspension of an agar culture, were introduced subcutaneously into the abdominal wall of a guinea-pig, an abscess shortly formed at the seat of inoculation and many of the bacilli were discharged with the pus. Dead tubercle bacilli have the same chemotactic power as the living organisms, and may also cause suppuration. When the number of bacilli is insufficient to provoke suppuration, they are taken up by the lymphatics and conveyed to the neighboring nodes, where the first signs of the disease appear. The number of infecting organisms probably has much to do with tuberculous infection, as an animal with an average vital resistance may be able to antagonize a number of organisms that could reach it under natural conditions, although it would be found to succumb should the number be increased beyond the limit.

The mode of introduction means much in tuberculosis. Tubercle bacilli introduced into abrasions and fissures of the skin, or admitted through punctured wounds, usually succeed in but limited invasions and provoke the purely local affection known as lupus vulgaris. When the bacilli fall upon the mucous membranes of the mouth and nose, it seems that, especially in childhood, the tendency is for them to be carried to the lymphatic tissues so that from the tonsils they reach the cervical glands, which become infected, and the disease makes slow progress from gland to gland along the cervical to the supraclavicular, then to the infraclavicular, then to the bronchial glands, and so ultimately reach the lung if its course is not checked. Infection through the intestine, probably because of the existence of some peculiarity of the lymphoid tissues in youth, takes place chiefly in childhood, the bacilli being transported to the mesenteric and retroperitoneal lymphatic glands.

Pulmonary infection may affect the lung directly, or the bacilli may find their way to the bronchial lymphatic glands in which they first develop, subsequently infecting the lung, either by continuity of tissue or by rupturing into some branch of the pulmonary circulation in which they are distributed to the lung.

Pelvic infection through the genital organs is usually advanced at the primary seat of disease before it makes inroads upon the pelvic and retroperitoneal glands.

Animals vary considerably in susceptibility. Rodents seem to be the most susceptible animals. Herbivorous animals are much more susceptible than carnivorous animals. Wild animals in confinement are more susceptible than wild animals at large.

Concerning the individual susceptibility among certain species of animals, our knowledge is defective. We look upon it as " some physical weakness," " a general run down of vitality," etc., but the nature of it is entirely obscure.

It seems probable that in many cases the accidents of infection have as much to do with the course of the disease as any peculiarities of the individual. Thus, should the infecting organism be exceptionally virulent, the result of its entrance into a tissue will be different from the result produced by an organism of very mild virulence. Should a number of organisms enter together or in rapid succession, their combined effects, especially if scattered, might be more difficult to overcome that the effects of a single bacillus.

Should the bacilli fall at once upon some tissue whose vascularity, richness in lymphatics, free supply of oxygen, and general looseness of texture all favored growth and distribution, the effects could not fail to be very different from those produced by the same organism in a dense, badly nourished tissue with few lymphatics.

Too much attention cannot be paid to these accidental conditions when considering vital resistance, and a person in the greatest physical vigor might succumb in consequence of them, when another in very poor condition might succeed in withstanding an entirely different form of infection.

The invasion of the body by tuberculosis is accomplished—(1) By continuity of tissue; (2) by lymphogenic metastasis; (3) by hematogenic metastasis; (4) by aërogenic metastasis; (5) by direct implantation.

1. *Continuity of tissue* favors the spread of tuberculosis from the primary nidus of infection. The conditions favorable to it are looseness and moisture, which enable the bacilli to grow unrestrainedly. It is by continuous

growth that tubercles increase in size, and that outlying or daughter tubercles are formed. *Contiguity* of tissues and organs also favors the spread of the disease, although the preliminary steps really transform the tissues in such a manner as to make the real process one of continuity. Thus, a tuberculous lesion of the lung, by establishing a chronic inflammatory reaction, causes the adhesion of the lung to the chest and thus favors the extension of the tuberculous process to the parietal pleura.

2. *Lymphogenic metastasis* is almost invariable in tuberculosis. Exactly by what mechanism the bacilli pass from the primitive lesion to the lymphatic nodes is not known. From the study of microscopic sections it seems probable that it is largely a matter of transportation by phagocytes, although direct transportation of free bacilli may occur.

3. *Hematogenic Metastasis.*—This may be the means of primary infection if we admit the possibility of tubercle bacilli ingested with the food being absorbed by the lacteals, conveyed through the thoracic duct to the venous system, and so thrown into the pulmonary and systemic circulations.

There is, however, a far more frequent means of hematogenic infection than this—that is, the inclusion of a vein in a tuberculous lesion, the erosion of its wall, and the entrance of bacilli directly into the blood-stream. This is known to take place in tuberculosis of the bronchial lymphatic nodes, in disease of other lymphatic nodes, and in pulmonary lesions. A uniform distribution of tubercles throughout both lungs indicates pollution of the pulmonary circulation by micro-organismal emboli which fail to pass through and enter the systemic circulation. It is, however, probably rare that the miliary tuberculosis is confined to the lungs, the tubercles in the remote organs simply being fewer and smaller, and hence less obvious than the pulmonary tubercles. When large numbers of tubercle bacilli succeed in entering the circulation and many fail to be impeded in their passage through the lungs, general miliary tuberculosis occurs.

4. *Aërogenic metastasis* takes place only in pulmonary tuberculosis. It is easily understood that when a tuberculous lesion exists in a lung and, by necrosis and softening, effects a communication with a bronchial tube, the entrance and exit of the air carry the infectious contents of the tube first in one and then in the other direction, until it is distributed not only along the primarily invaded tube, but into many of its smaller branches, and into the larger tubes and trachea. The entrance of this infectious material into new tissue areas may cause tuberculous, lobular, or bronchopneumonia, both in the primarily affected lung and in its fellow.

5. *Implantation* tuberculosis occurs from infectious material in transit through the trachea, larynx, pharynx, and mouth, and sometimes through the esophagus, stomach, and intestines, in any or all of which organs bacilli may lodge.

Varieties of Tuberculosis.—Single tuberculous masses of the brain are called *tyroma*. Clusters of tuberculous nodules, such as occur upon the pleura of cattle, are called "pearl disease."

The primitive lesions of tuberculosis are called *miliary tubercles*. A wide-spread distribution of such lesions is known as *miliary tuberculosis*, a universal distribution, as *general miliary tuberculosis*.

The common form of the disease characterized by marked caseation is known as *caseous tuberculosis*; the chronic form, with connective-tissue induration, as *caseofibroid tuberculosis*; the extremely chronic form, with marked cicatricial formation and induration, as *fibroid phthisis* or *tuberculosis*, and the rapid tuberculous pneumonia, as *caseous pneumonia*.

Morbid Anatomy.—The characteristic lesion of tuberculosis is the *tubercle—the miliary tubercle of Laennec*. It is a minute inflammatory and degenerative nodule which forms about the tubercle bacillus. The disease always begins with the formation of a miliary tubercle, whatever may be its future course.

As soon as the miliary tubercle attains a size permitting its recognition by the naked eye, it appears as a minute, grayish, translucent point. As time passes it increases in size by eccentric growth and the formation of outlying daughter tubercles until it reaches that of a pin-head or small pea. This is then called the "crude tubercle" of Laennec. The tubercle continues gray so long as it remains cellular in composition, but in most cases coagulation necrosis takes place at the center and causes it to become yellowish. The growth continues at the periphery while degenerating in the center, so that the lesions, if few in number or single, may attain a large size. It is not unusual to find single tuberculous masses, as large as pigeons' or even hens' eggs, in the brain, liver, spleen, and other organs. They always begin as miliary tubercles, but increase by the continuous formation of daughter tubercles at the periphery. These large tuberculous masses may have solid grayish substance, or if the degeneration has been more rapid, creamy yellowish contents.

They are rarely circumscribed by any definite boundary, but tend to infiltrate by the formation of outlying tubercles formed in the immediately surrounding tissue, showing invasion by continuity of tissue. When the number of tubercles is great, they do not become large, possibly because the function of the organ is suspended before time enough has elapsed. The patient dies, possibly because enough bacterial or metabolic poison is produced to kill him before extended growth is possible. It is in the lung that the most numerous and largest lesions are observed.

There is no essential difference between tubercles in different organs or tissues, other than can be accounted for by the peculiarities of the tissue.

The lesions sometimes depart from the usual type, as when suppuration is produced by the injection of large numbers of bacilli, and under less well-understood conditions in the pleura, pericardium, etc., where considerable purulent collections occur in which tubercle bacilli are more often absent than present, yet in which no other cause for the suppuration can be found. Rapid inflammatory infiltration and edema may occur in rapidly spreading pulmonary tuberculosis, with lesions much like those of croupous pneumonia, or scattered consolidated patches of bronchopneumonia may be observed. At times these diffuse infiltrations degenerate about as rapidly as they are formed, and a cheesy pneumonic condition is formed.

In tuberculosis of the bones and joints the amount of actual tubercle formation is greatly outweighed by the extensive puriform accumulations—cold abscesses—that make their appearance.

In cases of slow course and prolonged duration a fibroid change takes place. This is seen in the lymphatic tuberculosis common in cattle and occasionally seen in man, in which the affected nodes are transformed into enormous fibroid masses much more closely resembling a fibroma or a cicatrix than a tubercle.

Some forms of the disease are almost purely cellular, and although of slow growth, lead to the formation of translucent nodules upon the serous membranes, which, because of their appearance, have been described as "*pearl disease*." This form of tuberculosis is common in cattle, but may also occur in man. The lesions, which are more frequent upon the pleura than upon other serous membranes, form clusters of rounded, grayish-pink, translucent, soft, polypoid excrescences, some of which may be as large as a hen's egg, although rarely larger than currants or grapes.

Old tuberculous lesions that have ceased to grow appear completely circumscribed by dense encapsulated connective tissue, and show disorganization of the internal structure, either by complete caseation or by calcification with the transformation of the caseated mass into a chalky deposit. Large and small nodules of this kind are quite commonly found in the lungs of persons who have died from other causes, and can usually be regarded as evidences of "healed tuberculosis." They appear as distinct puckers upon the pleura, when near the surface. Sometimes they occur in the deeper structure of the lung. In nearly all cases of this kind the number of calcified lesions is small, the size smaller than a pigeon's egg and rarely larger than a pea.

Pathologic Histology.—The tubercle bacillus having become lodged in a nidus appropriate for its growth, progressively increases in numbers and hence in its irritative and poisonous powers. The classic experiments of Baumgarten upon tuberculosis of the iris in rabbits led him to believe that the first changes produced by the bacillus were to be found in the fixed connective-tissue cells of the part, which increase in number and thus form the primitive tubercle. No doubt almost immediately following this effect upon the connective-tissue cells the chemotactic influence of the bacillus is felt, and the cellular collection receives additional cells from the blood vessels. According as the local irritative influence or chemotactic influence predominates, the tubercle will be *lymphoid*—that is, will consist of lymphoid cells, mostly leukocytes—or *epithelioid*—that is, consist chiefly of epithelioid cells.

A primitive tubercle, therefore, consists of cells derived partly from the connective tissues and partly from the blood vessels. The tubercle bacilli are continually multiplying and the number of cells in the tubercle continually increasing.

The cells of the tubercle require nutriment, but in the tuberculous inflammation no new blood vessels form and hence no increase of nutriment is provided. Not only are no new blood vessels formed in the tuberculous tissue, but the capillary blood vessels of the part in which it forms are destroyed as it advances. Tubercles are, therefore, continually avascular, so that before they attain any considerable size the older parts—that is, those first formed and centrally situated—show signs of degeneration and disintegration (coagulation necrosis). While the peripheral part of the tubercle is growing, the central part is degenerating. In addition to the avascularity by which the death of the central portion of the tubercle is brought about, the tubercle toxin is no doubt responsible for some of the local damage. Chemic analyses have shown that the bodies of the tubercle bacilli contain an extremely irritating substance allied to the fatty acids. Dead tubercle bacilli as well as living organisms contain this irritating substance in their bodies, and when disseminated through the circulation, are capable of producing minute tubercles.

Histologically each tubercle may be divided into three zones: a central zone, which usually consists of a mass of coagulation necrotic, disintegrating material, composed of destroyed cells and dead bacilli; a median zone, consisting of epithelioid cells, and usually containing one or more giant-cells, and a peripheral zone, in which occasional epithelioid cells are mingled with a considerable number of round-cells of hematogenous and connective-tissue origin.

These three zones really represent three different developmental stages: The outer zone, the earliest stage, where a mingled multiplication of connective-tissue cells and round-cell infiltration can be observed; the median zone, a later stage, in which attempted organization and recovery of the inflammation have gone on far enough to form epithelioid cells, which sometimes undergo a monstrous development with the formation of characteristic giant-cells, and the central zone, the oldest part, in which the vitality of the tissue has been destroyed and the cells have died.

It is impossible to determine exactly the origin of the giant-cell. By some it is looked upon as an overgrowth of the epithelioid cells, multiplication of whose nuclei takes place more rapidly than that of the protoplasm. My own impression has always been that the giant-cells are formed by the coalescence of partly degenerated epithelioid cells, and is, therefore, a retrogressive formation.

The histology of the tubercle varies considerably according to the rapidity of its growth and the resisting power of the individual. Thus, if the patient be highly susceptible and the disease progress rapidly, the probabilities are that the lesion will partake largely of the nature of the small round-cell infiltration, with rapid coagulation necrosis. If, on the other hand, the patient be ordinarily resistant, the appearances will be those above described, and in case the vital resistance of the individual is marked, the tendency will be for repair to progress more rapidly than destruction, so that a considerable number of the epithelioid cells will be transformed into connective-tissue fibers. These variations in the resistance of the individual and the consequent differences in the histology of the lesion have caused the tubercles to be divided microscopically into the *lymphoid*, *epithelioid*, and *reticulated*.

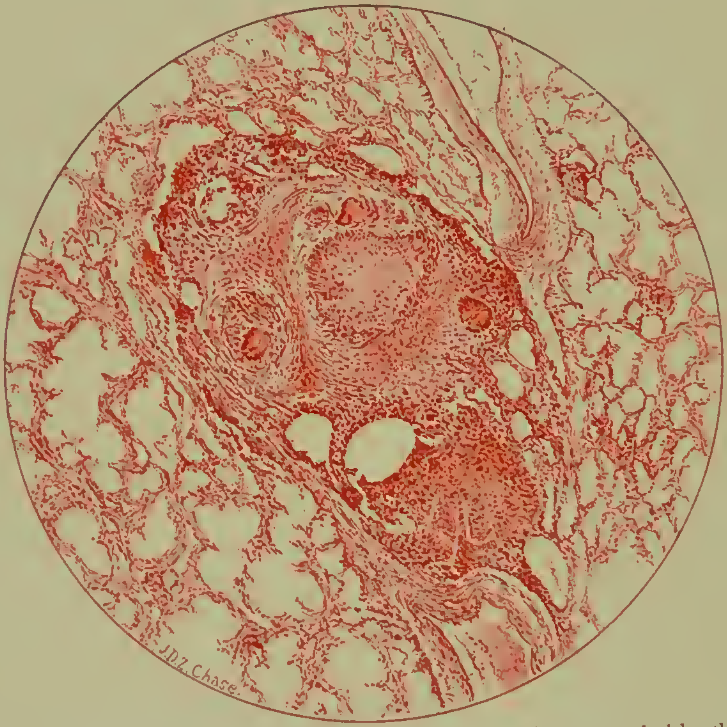

FIG. 209.—A miliary tubercle of the lung, consisting of two, probably three, submiliary tubercles. The coagulation necrosis of the center and the giant-cell formation are well shown (× 70).

Some pathologists have regarded these different forms of the tubercle as having a different etiology, and Gibbs at one time contended that the tubercle bacillus, while the cause of the cellular or lymphoid tubercle, was continually absent from the reticulated tubercle. Reticulated tubercles are, however, nothing more than those in which the preëxistent fibers of the tissues have not been destroyed, or in which the formation of new fibers has taken place from epithelioid cells and fibroblasts. Why the fibers in tubercles sometimes have a radiated appearance is not understood. It may in some cases depend upon contraction caused by the reagents in which the tissue is hardened for microscopic study. But this will not explain all cases, for not only is the radiation observed in the fibers of the connective tissues, but also sometimes in the epithelioid cells surrounding the areas of necrosis which have their long axes in the lines of the radiation, so as to appear, as some one has said, "like an army with bayonets" opposing the advance of the caseation into the surrounding tissue.

Sometimes the contrast between the anuclear caseous central zone and this line of surrounding epithelioid cells is so marked that the appearance is described as like a "*raked field*." The caseated areas may show anuclear homogeneous masses, corresponding in size and shape to cells that belonged to the preëxistent tissue in which the tubercle developed. When the caseation advances further, these cell-bodies become broken up into hyaline fragments of irregular shape. And still later the cheesy material becomes slightly granular, yellowish or almost colorless, and no details can be made out.

The coagulation necrosis seems to attack first the cells belonging to the tissue; next, the leukocytes; and lastly, the epithelioid cells.

The giant-cells may occur in the center of the small tubercle, and thus represent the earliest transformation of epithelioid cells, into what is later to form the cheesy center. Usually they are found in the intermediate zone. They may be very large, a single giant-cell sometimes seeming to make up the entire tubercle, or they may be smaller and numerous. At one time the giant-cell was thought to be characteristic of tubercle, but it has long since been shown that giant-cells occur in other specific granulomata and in simple inflammation, and are common in sarcoma. The form most common in tubercle, and in fact seldom met elsewhere, is that first pointed out by Langhans as "Riesenzellen mit wandständigen Kernen." In this form a large spheric cell presents a necrotic center, and has its nuclei, of which several hundred may be present, arranged like a wreath about the periphery. When, because of pressure, the giant-cells are elongated, the nuclei may be clustered at the poles or form an equatorial belt. The most probable explanation why the nuclei assume these particular positions in the cells is that, as degeneration begins in the central part of their protoplasm, the nuclei move away and occupy the still well-nourished area.

The tubercle bacilli usually have a definite distribution in the tubercle. The original tubercle formed about the originally present tubercle bacilli, but as the tubercle grows, the bacilli increase in number and distribute themselves over a greater surface, the older bacilli near the center dying. As the tubercle continues to increase in size and degenerate in the center, the older bacilli occupying the central area probably die and disintegrate, while their progeny occupy the new and developing portions of the lesion. It is because of this multiplication of the bacilli that the disease continues to invade fresh areas, and no other explanation need be given than this relationship of bacilli to lesion to make clear why tuberculosis should be a continually progressing and disintegrating disease.

Tuberculosis is not limited to the primary seat, but is prone to metastasis by the transplantation of the bacilli from the primary to the secondary areas. This takes place in part through the activity of phagocytic cells, which take bacilli into their cytoplasm for the purpose of destroying them, and carry them through the tissue to slightly removed positions, or continue with them as far as neighboring lymphatic glands, or even to the systemic circulation.

The bacilli may also be swept away from the tubercle by currents of lymph. In whichever way metastatic distribution occurs, it always results in the invasion of some new part of the body in which the bacilli lodge and reproduce the changes already described.

The majority of the bacilli are not transported any considerable distance, so that new tubercles are usually formed adjacent to the older ones: so close, in fact, that it not infrequently happens that their subsequent increase in size causes them to coalesce and form a single large tuberculous mass. Such a mass is said to consist of *submiliary tubercles*. The large masses undergo the cheesy change, soften, and evacuate, forming cavities or ulcers when contiguous to a surface from which the products of degeneration can be discharged.

It rarely happens that tuberculosis occurs in any part of the body without metastatic invasion of the lymphatic glands. Thus, in tuberculosis of the lung the bronchial lymphatic glands are usually infected, and in intestinal tuberculosis the mesenteric and retroperitoneal glands are affected. In the secondary lesions and lymphatic glands the disease may progress more rapidly than in the primary seat of disease. Such lymphatic lesions, when situated where invasion and erosion of blood vessels are possible, may discharge their contents into the veins, thus liberating numbers of bacilli into the systemic circulation.

Recovery of Tuberculosis.—Tuberculosis probably recovers much more frequently than is usually supposed, but not without leaving visible changes in the tissues. Postmortem examinations show recovery in about 20 per cent. of cases of tuberculosis, though such cases are seldom known to have been tuberculous during life. How complete the recovery is must always remain a question, for it occurs by exclusion of the tuberculous process rather than by its eradication. The disease recovers because the vital resistance of the patient enables the process of repair to outweigh that of destruction. The tubercle bacilli thus become encapsulated in a mass of growing connective tissue which surrounds the tubercle and prevents its advance. This can happen only, however, when the susceptibility of the individual becomes changed, and it must not be misunderstood that the cessation of the growth of the tubercle depends upon the connective-tissue formation. It is only when the resistance of the individual is so increased as to make it possible for the tubercle bacilli to be successfully combated that the encapsulating process can occur.

The connective tissue formed about the recovering tubercle hastens the absorption of its disintegrated elements by contracting upon the diseased tissue. When absorption is impossible, calcareous infiltration is likely to take place, and the once cheesy area becomes transformed into a chalky mass.

The fate of the tubercle bacilli in these areas is of interest. They presumably remain vital but a short time, as, so far as is known, they have no spores or permanent forms. It seems, however, that within circumscribed and encapsulated areas in which no known tuberculous process has gone on for years, a sudden outburst of bacillary invasion may follow an injury or inflammation, so that from an old Pott's disease or from a calcified area in the lung a sudden and fatal tuberculous disease may originate.

Physiology.—That tuberculosis is associated with marked constitutional involvement is evident in nearly all cases. Exactly what the source of damage is has not been determined, as no important toxic substance has yet been extracted from the tubercle bacillus. In all cases of wide-spread tuberculosis, however, whether of the lungs, the bones, the lymphatic glands, or other organs, fever, cachexia, anemia, and amyloid and fatty degenerations may be expected.

Symptoms.—Fever.—The fever of pure tubercular infection is usually moderate in severity,—101°–102° F.,—with nocturnal exacerbations. It is irregular, persisting for a time, disappearing more or less completely for a time, and then reappearing.

When hectic fever or hyperpyrexia accompany tuberculosis, accidental complicating or secondary infections may be expected.

This fever sometimes makes its appearance in an intermittent form, with regular fluctuations simulating malaria, the pyrexial periods being accompanied or succeeded by sweats. Sweating—especially nocturnal sweating—is very common in tuberculosis.

Cachexia develops in chronic tuberculosis. The patient emaciates, the skin becomes pale and white, the fingers enlarge at the tips, and the nails curve over them (drum-stick fingers). As the disease progresses the emaciation may become extreme.

The **anemia**, which is probably the cause of the cachexia, is a secondary or symptomatic anemia, with diminution in the number of erythrocytes and percentage of hemoglobin. In uncomplicated cases there are no positive changes in the leukocytes by which the disease can be diagnosticated. Some writers lay stress upon variations in the percentage of lymphocytes, but they are not characteristic. Cases complicated by secondary infections with pyogenic organisms usually show some leukocytosis.

The anemia is progressive and increases up to the time of death. It probably never is dangerous in itself.

Fatty infiltration of the liver is frequently seen in fatal cases, the infiltration depending upon nutritional disturbances. The liver is very large, pale in color, firm in texture, and beautifully "nutmeg" in appearance. It is usually anemic.

Amyloid disease is not uncommon in advanced tuberculosis both of the lungs and of the bones and joints. All grades of it are seen, from changes so slight as to be detected only by the microscope, to complete involvement of the principal organs.

LEPROSY.

Leprosy is a specific, infectious, doubtfully contagious, inflammatory disease, caused by the *Bacillus lepræ*, and characterized by nodular lesions of the skin, subcutaneous tissues, nerves, and occasionally of the internal organs. The disease has been recognized for many centuries, having been known in the time of Moses, who introduced into the laws of the people of Israel specific directions for its recognition and for the isolation of the sufferers. In early times, however, numerous other skin affections were confounded with it.

It is a rather frequent disease in warm countries. In China and India it is common along the coast, and it is frequently seen in Syria and along the north coast of Africa. In Europe it occurs with some rarity along the Mediterranean coast and along the Atlantic coast of Scandinavia. Occasional cases occur in North America, usually along the Gulf coast of the United States, in Acadia, New Brunswick, and Mexico. Many of the cases are imported from China and South America. On the Pacific coast it occurs chiefly among the Chinese emigrants. About two hundred years ago it was imported into the Sandwich Islands, where it has become a veritable scourge.

Etiology.—Lepra is caused by the Bacillus lepræ of Hansen, which is found in immense numbers in the nodular lesions and in the nasal discharges.

The lepra bacillus closely resembles the tubercle bacillus in morphology, being about the same size and shape. It also stains like the tubercle bacillus, resisting ordinary staining solutions, but staining deeply with solutions containing a mordant, and subsequently resisting the action of mineral acids. The successful cultivation of the bacillus has been claimed by a number of investigators, though it is not recognized as possible. It is pathogenic only for man, inoculation experiments upon the lower animals having uniformly failed. At least one successful inoculation has been made upon a man—a condemned criminal in the Sandwich Islands.

In their grouping in the tissues the lepra bacilli differ from the tubercle bacilli, not being sparingly distributed throughout the diseased tissue, but being present in immense numbers, especially in the interior of certain large cells known as the "*lepra cells.*" In the nodular form the bacilli occur in large numbers in the lymph-spaces and in the lepra cells; in the anesthetic form, in the sheaths of the nerves.

The disease spreads slowly because of the purely parasitic nature and comparatively feeble resisting powers of the bacillus, yet free association with lepers has been followed by infection in several of those whose philanthropic labors have been among them, notably in the case of Father Damien, who was their missionary for many years in the Sandwich Islands.

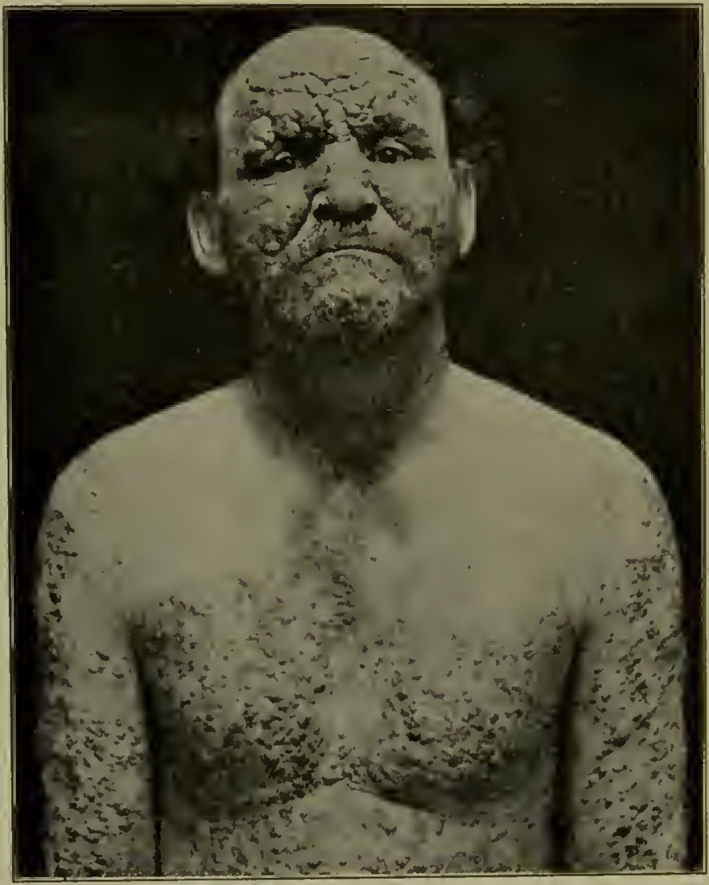

FIG. 210.—Case of nodular leprosy (from a patient of Dr. John V. Shoemaker's in the Medico-Chirurgical College, Philadelphia). The leonine expression is well shown.

Infection may occur—(1) By direct inoculation, either experimentally, as in the case of the criminal above referred to, or accidentally by fingers and other objects soiled with the discharges from the nose and ulcers. (2) It may also occur by intimate personal relations, through kissing and sexual intercourse. (3) It may occur through fomites. Some have attributed the inoculation to the bites of insects, but proof of this is still lacking.

The appearance of the disease after inoculation is slow, the period of incubation sometimes extending over some months and the disease lasting for many years. Most cases continue for from five to twenty years before succumbing to intercurrent affections, the most frequent of which is tuberculosis. In uncomplicated cases death occurs from exhaustion. It is said that occasional cases recover.

Leprosy is not limited to any age. It is not known to be hereditary, but children and adults, young and old, suffer from it. It is chiefly a disease of the lower classes, among whom ignorance and carelessness regarding prophylactic measures prevail. It seems to attack the lower races more quickly than the Caucasians, but this may depend upon the habits and conditions of life rather than upon any racial predisposition. In Hawaii, where it is so exceptionally prevalent and severe, it is apparently true that certain peculiar customs of the people have favored its spread sufficiently to explain its frequency without making necessary any reference to the climate or peculiarity of the native constitution.

Two chief forms of the disease are described—**lepra nodosa,** or **elephantiasis græcorum,** and **lepra anæsthetica.** These may occur independently of each other or in combination.

Lepra Nodosa.—This form is characterized by the development of nodules in the skin and subcutaneous tissue of the face, usually beginning about the angles of the nose, and extending to the nose, lips, and forehead, and later appearing on the exterior surfaces of the arms and legs and upon the fingers and toes. The nodules vary in size, frequently ulcerate, and slowly cicatrize, with the formation of scar tissue, which distorts the countenance by the formation of seams and ridges corresponding to areas of ulceration, which make more conspicuous the projecting nodes. The entire face and ears may become affected, likewise the trunk and extremities, and occasionally the lepra nodes are found in the internal organs. The lesions of the internal organs associated with leprosy are, however, frequently tuberculous, as tuberculosis is common as a secondary infection in leprosy.

The lepra bacilli seem to gain entrance into the tissues through minute lacerations, no doubt very often being carried in by the finger-nail when scratching. This will probably explain the frequency of the occurrence of the disease about the nares, while its frequency about the mouth may depend upon the use of a pipe in common with others or by infected drinking-vessels.

Morbid Anatomy.—To the naked eye, the lepra nodules present upon section a grayish or yellowish, semitransparent, uniform appearance, similar to other inflammatory formations. The loose subcutaneous areolar tissue is most apt to be affected. Microscopically the nodules consist of several important elements. There are, first of all, large numbers of small, often vacuolated, epithelioid cells. These not infrequently contain bacilli, and are sometimes found in the lymphatic spaces from the endothelium of which they may be derived.

There are also large cells, known as *lepra cells,* which sometimes contain many nuclei, and numbers of vacuoles, some small and some large, and usually large numbers of the lepra bacilli. The lepra cells may also be found within the lymphatics. According to Metschnikoff, they are large mononuclear leukocytes that have taken up the bacilli.

Clumps of free bacilli can be found in the lymphatics and among the cells of the tissue. The fibroconnective tissue about the lesions is increased. From this description it will be observed that the lesions of leprosy lack the definiteness of tuberculosis, more closely resembling ordinary inflammations. The lesions of the internal organs consist entirely of fibrous patches. Chronic interstitial inflammations of all the organs are common. Nodes also occur in the lung, liver, spleen, and kidney, although the tendency is to regard the lesions of the internal organs as, for the most part, tuberculous.

The lesions of lepra nodosa, while nodular, are less well defined than those of tuberculosis, and are always much better vascularized and hence less apt to undergo coagulation necrosis. There is no caseation of the lepra nodes and the ulcerations depend as much upon traumatic injuries and secondary infections as upon retrogressive changes.

The first appearance of the nodes is frequently preceded by the occurrence of hyperemic spots, which disappear, leaving behind them pigmented areas, which begin to enlarge until a walnut-sized node may be formed. As has already been said, the nodes may remain isolated or may become confluent.

The enlargements consist of granulation tissue, which extend to the epiderm above, and deeply into the subcutaneous areolar and adipose tissues below. This tissue is quite prominent about the hair-follicles. The tissue between the bands of cicatricial tissue and cellular nodes is apt to atrophy; especially are the hair-follicles liable to be lost; on the other hand, it may be unaltered except by the existing hyperemia. The lepra nodes sometimes organize, sometimes soften and form ulcers, the ulceration usually taking place in consequence of external injury.

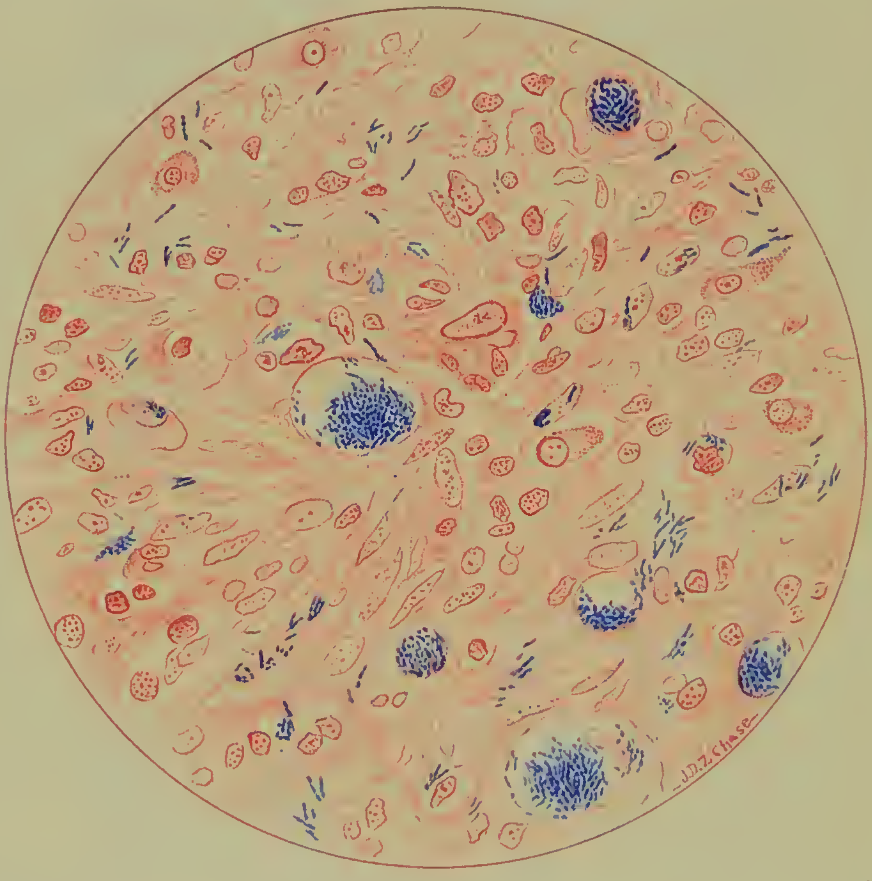

FIG. 211.—Section of one of the nodules from the patient shown in Fig. 210, stained by the Weigert-Gram method to show the lepra bacilli scattered through the tissue and inclosed in the large vacuolated "lepra-cells" (× 1000).

Not only is the skin affected, but also the mucous membrane of the eye, nose, mouth, larynx, and intestine, sometimes with the formation of circumscribed nodes, sometimes with the formation of diffuse cellular infiltration.

The appendages of the skin are involved, and the infection of the hair-follicles causes the hairs to become unusually coarse in texture, white in color, and few in number. In anesthetic leprosy the trophic distributions may also cause the occurrence of a *leprous vitiligo*.

In both forms of leprosy the lymphatic glands are swollen, dense in structure, and of yellowish-white color. The lymphatic glands of the first affected parts are first observed to enlarge, but the enlargement is not limited to those in the leprous areas, extending later to such internal glands as those of the mesentery. Many of the glandular enlargements may depend upon associated tuberculosis.

Lepra Anæsthetica.—This form of the disease is characterized by the growth of the bacilli in the sheaths of the nerves and the formation of cylindric or fusiform swellings, especially upon the ulnar and popliteal nerves. The result is neuritis, followed by the occurrence of hyperemic patches, which are sometimes swollen, in the areas of distribution of the affected nerves. These may be painful at first, but subsequently become anesthetic. Together with the anesthesia, paralysis of motion not infrequently occurs, followed by atrophy of the palsied muscles. The skin of the anesthetic patch is often the seat of a peculiar eruption, known as *pemphigus leprosus*. The bullæ which form may be dry, leaving pale anesthetic patches, or they may be followed by ulcers. Sooner or later these ulcerations, aided by accidental infections resulting from traumatism of the insensitive parts, are followed by loss of some of the phalanges of the fingers and toes, and deformity of the remaining portion of the member, by cicatrization.

Either form of the disease may be primary, or the two may occur simultaneously, or either form may be succeeded by the other. They are not different diseases, but different manifestations of the same disease—the one subcutaneous, the other nervous. The duration of the anesthetic form is said to be greater than that of the tubercular, and its recovery more ready, though serious deformities remain.

GLANDERS.

Glanders (Equinia; Farcy; Morve; Farcin; Rotz).—Glanders is an acute or chronic, specific, infectious, eruptive disease of horses and asses, occasionally seen in man and other animals as a result of accidental infection. It occurs among men whose occupations bring them into intimate association with horses, as hostlers, soldiers, etc.

Etiology.—Glanders is caused by Bacillus mallei or the glanders bacillus, discovered by Löffler and Schütz. There is no doubt of the specificity of the bacillus, as it fulfils all Koch's laws. Infection takes place from contact with diseased animals, the bacilli entering through minute abrasions, etc., of the skin or mucous membranes.

Morphology.—The bacillus is somewhat shorter and distinctly thicker than the tubercle bacillus. The ends are rounded; the bacilli may be joined in pairs, although usually single. Their substance sometimes shows irregularities which may be vacuoles caused by involution changes. The organism is not motile and has no flagella. It forms no spores. It stains well with aqueous aniline dyes, but not by Gram's method. It is difficult to stain in tissue, as it readily decolorizes.

Cultivation.—The artificial cultivation of the bacillus is very simple, as it grows readily in nearly all the culture media, at temperatures ranging from 25° to 42° C. It is, however, a slow grower. The best method of isolation from suspected purulent matter is that of Strauss, who recommends that the suspected matter be introduced into the abdominal cavity of a male guinea-pig. In three or four days the disease becomes established and enlargement of the testicles is observed. A few days later, if the animal be killed, abscesses are found in the testicles, from the pus of which pure cultures of the bacillus can be secured. The guinea-pigs, if not killed, die spontaneously in about two weeks, with wide-spread pyemia and suppurating joints.

Gelatin is not an appropriate culture medium, as the temperature at which the growth takes place is high enough to liquefy it. The glanders bacillus does not liquefy gelatin.

Upon agar and glycerine-agar the colonies which form are discrete or confluent, moist, shining, somewhat viscid, circumscribed, and grayish. In tube cultures upon glycerin-agar a thick, luxuriant, homogeneous, grayish, shiny mass without any marked differential characteristics forms. The growth upon blood serum is similar and lacks peculiarities. In bouillon the growth clouds the medium for a time, a pellicle forming upon the surface, and a sediment collecting at the bottom of the vessel. In milk, acidity accompanied by firm coagulation occurs.

The classic characteristic of the glanders bacillus is the peculiar appearance of the growth upon potato, which resembles a drop of honey, and is accompanied by a greenish-brown discoloration of the potato itself for a considerable distance about it.

The virulence of the bacillus slowly wanes if kept long upon artificial media. Its resisting powers are slight. It is not killed by thorough drying, but is destroyed by five minutes' exposure to 55° C. By 1 : 5000 bichlorid of mercury solution it is killed in two minutes, and by 1 : 20 carbolic acid solution in five minutes.

Pathogenesis.—The organism is most pathogenic for field-mice; next most virulent for guinea-pigs. It also infects man, horses, asses, sheep, pups, and other animals.

In field-mice the disease at once assumes the form of a rapidly fatal septicemia and kills the animal in a couple of days. In guinea-pigs it is less rapid and is characterized by extensive local necrotic and suppurative lesions with pyemia. It is usually fatal in about two weeks.

In horses, asses, and mules the disease runs either an acute or a chronic course, the lesions of which will be described below. In man it is usually an acute febrile affection which may simulate typhoid fever until the lesions of the skin and mucous membranes present themselves; sometimes it is chronic and lasts for months.

Morbid Anatomy.—In spontaneous glanders of horses the ordinary point of inoculation is the Schneiderian membrane of the nose, in which small cellular nodules the size of millet-seeds and peas are formed. These gradually increase in size for a considerable time, then soften and ulcerate, leaving ragged ulcers with yellowish, elevated, infiltrated borders, which slowly increase in size, and not infrequently unite with neighboring ulcers by the erosion of the tissue between. The ulcers discharge a slightly blood-stained pus, which contains bacilli. They may heal with the formation of stellate scars. The lymph-glands of the neck invariably enlarge and inflame. Pyemic abscesses of the skin and of the subcutaneous and intermuscular tissues are very common; suppuration of the joints may occur. Abscesses of the internal organs are not infrequent. The respiratory and pulmonary mucous membranes are more or less affected by the inspiration of infectious material. The fever becomes high as the disease advances, symptoms of prostration appearing early. Death occurs with all the signs of septic poisoning.

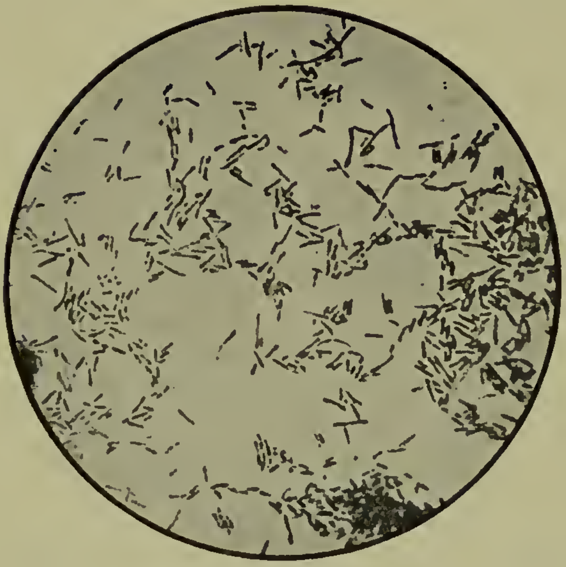

FIG. 212.—Bacillus mallei, from a culture upon glycerin-agar (× 1000) (Fränkel and Pfeiffer).

Glanders of the lung in its macroscopic appearance may resemble tuberculosis, occurring in the form of scattered inflammatory foci—*i. e.*, bronchopneumonic patches. Interstitial inflammations of the lung also occur, but the bronchopneumonic form seems to be the most frequent, and probably results from the direct inhalation of the bacilli into the air-cells.

The bronchopneumonic patches are originally of a reddish color, but become pale in the center, and take on a more or less distinctly yellow color as the cellular nodules soften and suppurate. The surroundings of the patch are frequently grayish-white, and have somewhat the appearance of bacon. This transformation depends upon fatty degeneration of the central portion of the exudate and reactive inflammation about the periphery of the node. As the destruction progresses, larger or smaller necrotic areas with foul purulent contents may be formed; or the contents may be absorbed, and secondary contraction of the newly formed connective tissue take place, so that the lobule becomes transformed into a small fibroid mass. The interstitial form of pulmonary disease probably results, as in tuberculosis, from the dissemination of the bacilli by the lymphatics.

Pathologic Histology.—Histologically, the glanders nodules consist of a dense accumulation of small round-cells, with numerous epithelioid cells at the periphery. Giant-cells, such as are seen in tuberculosis, do not occur. In certain cases, known as *farcy*, the disease affects the skin, beginning with the formation of small miliary nodules the size of peas or hazel-nuts in the papillary layer of the skin. These nodules are known as "*farcy buds*," and are characterized by a marked tendency to rapid central necrosis, suppuration, and the formation of deep ulcers. Glanders of an internal organ is usually embolic in character, and characterized by the formation of nodules about the size of a pea, consisting chiefly of lymphoid cells, with occasionally epithelioid cells at the periphery. In the course of time they may be transformed into shrunken fibroid or calcareous masses. Occasionally, instead of this nodular form, the disease assumes the character of diffuse cellular infiltration, with final suppuration or formation of cellular granulation tissue.

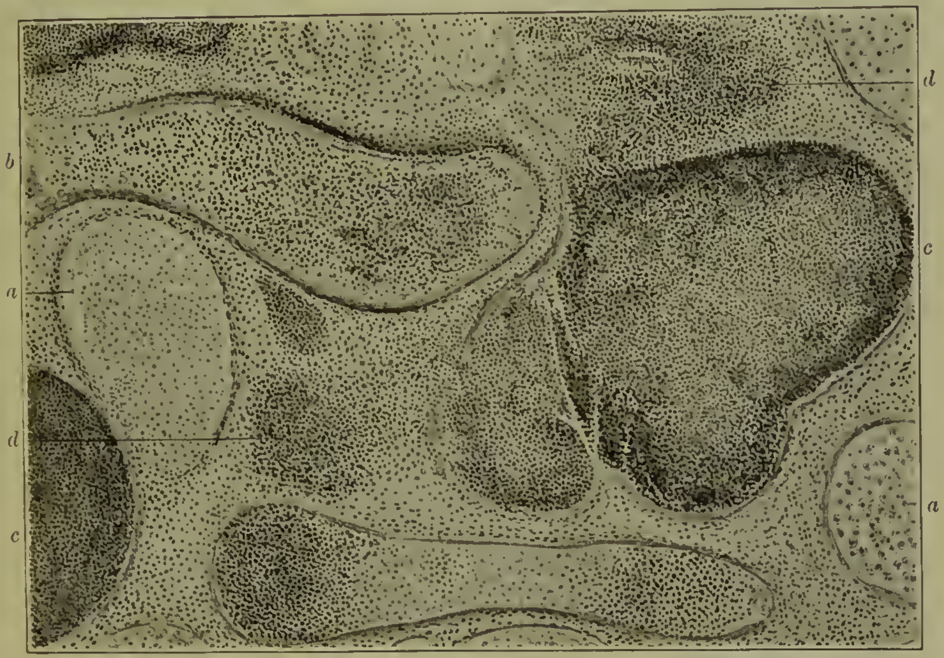

FIG. 213.—Glanders lesion: *a, a*, Seminiferous tubule; *b, c, c*, tubules filled with leukocytes; *d, d*, mass of leukocytes in the tissue (× 100) (Ziegler).

The disease in man is less rare than is usually imagined. The infection may take place through the conjunctiva, the nose, and wounds of the skin, to which the infectious discharges from the nose of a horse have been accidentally brought. The disease as seen in man is usually an *acute* febrile affection, suggestive of typhoid fever or some other septic process. An eruption of pustules usually occurs upon the skin, which subsequently form persistently enlarging ulcers, of a phagedenic character, with a dirty-grayish, pus-discharging background. It is usually fatal.

Lymphangitis with phlegmonous infiltrations of the intermuscular tissues, lymphadenitis, and glanders of the internal organs succeed the primary superficial lesions.

Chronic glanders in man is more rare and is characterized by slowly extending and cicatrizing ulcers. In about 50 per cent. of the cases chronic glanders recovers, although not until extensive injury has been done.

Actinomycosis (Lumpy Jaw; Big Jaw; Swelled Head; Wooden Tongue; Clyers; Strahlenpilzkrankheit).—Actinomycosis is a chronic, contagious, inflammatory, and degenerative disease of cattle, caused by the Actinomyces bovis, discovered by Bollinger in 1877, and characterized by nodes of granulation tissue, with necrosis, sinus formation, and new fibroconnective-tissue formation, usually affecting the jaws, tongue, and internal organs.

Actinomycosis is most commonly a disease of cattle, especially of calves, though it occasionally occurs in man.

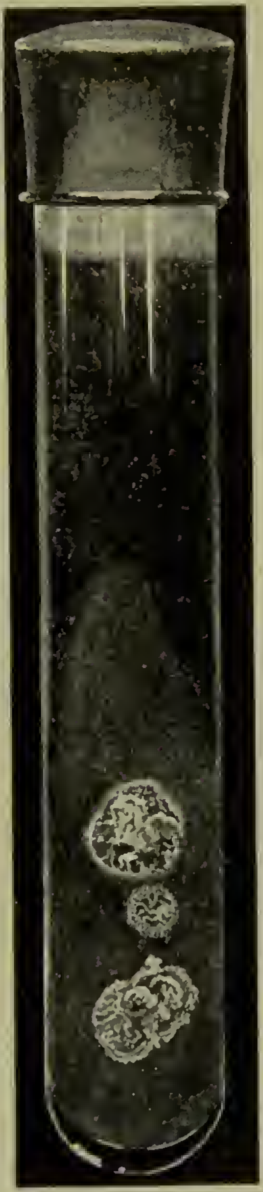

FIG. 214.—Actinomycosis; glycerin-agar culture. Limpet-shaped colonies three and a half months old (Curtis).

Etiology.—Actinomycosis is caused by the interesting fungus known as the Actinomyces bovis. It is of sufficient size to be observed by the naked eye in the pus and granulation-tissue nodes, as "sulphur-grains"—*i. e.*, sulphur-yellow bodies about the size of a pin-head. Such an entire fungous mass when examined microscopically is found to consist of several zones embracing entirely different elements. At the center is a mass of granular substance containing numerous bodies resembling chains of cocci and spores. Extending from this center outward is a radiating mass of branched, thickly tangled mycelial threads which terminate in an acute zone of conspicuous rays or club-shaped bodies, large and radially arranged, forming the most conspicuous part of the fungus. When artificially cultivated, fungi are crushed, and, examined under the microscope, it is found that the clubs are the expanded ends of the mycelial threads. What the function or purpose of the characteristic clubs can be is not settled. Some regard them as reproductive organs, some as involution forms.

The fungus is not motile. Its spores are unknown. It stains well by all methods, including Gram's method.

Cultivation.—The fungus can be artificially cultivated outside of the body, and grows upon a variety of media at room-temperature as well as at 37° C., though more slowly at lower temperatures. It grows best when it receives a plentiful supply of oxygen.

Upon all the culture media the organism grows with the formation of rounded bodies suggesting the "grains" or "rays" found in the lesions, but lacking the typical clubs, and showing the roset form less well in consequence. The rounded masses are often umbilicated, may have a yellowish color, and show delicate aërial filaments upon the surface; old growths may have a white dust upon them. The colonies cling tenaciously to the surface of the media upon which they grow. When planted in raw eggs, no nodular masses occur, but a delicate, frequently branched, filamentous growth develops.

The most luxuriant growth takes place upon blood serum, which is slowly liquefied. Gelatin growths are peculiar and arborescent; the gelatin is liquefied.

Upon artificial media in the laboratory the organism loses its virulence.

Pathogenesis.—Attempts to infect the laboratory animals with the actinomyces usually fail. The introduced parasites are either absorbed or become encapsulated. Peritoneal actinomycosis of rabbits is occasionally achieved, nodules with the essential peculiarities appearing in the omentum, mesentery, and elsewhere.

Source of Infection.—The native habitat of the fungus is unknown, and we are acquainted with it only as it appears to us in the tissues of the diseased animals and in our cultures. It is supposed that infection takes place through food, because it so regularly occurs first in and about the mouth, and, indeed, one case has been traced to a puncture of the pharyngeal wall by a barley spikelet. The infection seems not infrequently to occur through carious teeth, and more frequently occurs in the lower than in the upper jaw. Of 73 cases collected by Morsbruegger, the jaws, mouth, tongue, throat, or esophagus was involved in 41; the respiratory tract in 14; the intestines were involved in 11, and the point of infection was not determined in the remaining 7.

Occurrence.—The disease occurs in cattle and in man. It is unknown among carnivorous animals. It may occur in any part of the world.

Morbid Anatomy.—The disease is characterized by the formation of granulation-tissue nodes and abscesses, in the center of which the ray-fungus is usually found. In the majority of human cases toothache was first complained of; subsequently a swelling formed at the root of the tooth, and subsequent infection of the jaw-bone occurred. The disease for some time remains localized, and an abscess is apt to form, discharging a creamy-looking pus containing small yellowish granules. When allowed to go on, the bone becomes riddled with sinuses, communicating with each other and with the exterior. Israel states that the actinomycotic tumors are apt to migrate, and illustrates with a tumor which occurred on the alveolar process of the jaw, descending later to the submaxillary region, from which it disappeared subsequently to form a large swelling below the hyoid bone, and after this had been opened and treated, another just above the clavicle. Human beings sometimes recover if treatment is prompt and radical, but not infrequently the disease pursues the same course as in cattle.

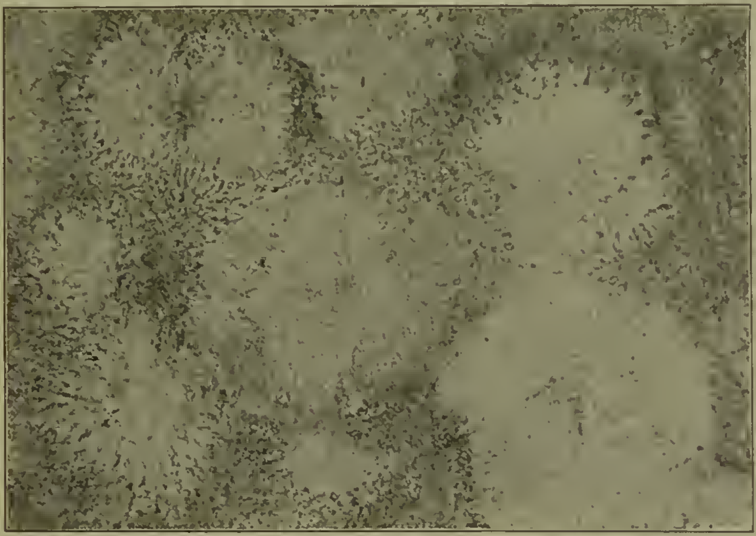

FIG. 215.—Actinomyces granule crushed beneath a cover-glass, showing radial striations in the hyaline masses. Preparation not stained; low magnifying power (Wright and Brown).

The infection of the respiratory apparatus produces a chronic disease of the lungs, with purulent bronchitis, patches of peribronchitis, and bronchopneumonia. The lesions are yellowish white in color and suppurate. Hemorrhages from the capillaries are frequent, and the lung becomes riddled with small cavities containing pus, fragments of degenerated tissue, and parasites, as well as granulation-tissue nodes of grayish-yellow color which have not yet softened.

The sputum in these cases is mucopurulent and contains the fungi. The lung tissue in the neighborhood of the disease is consolidated, infiltrated with small round-cells, and likely to be deformed by cicatricial bands. Pleurisy is common and may be adhesive, so that the lung is bound firmly to the chest-wall, which subsequently becomes invaded, riddled with sinuses, and permits the escape of the purulent contents through external openings. Or if the pleuritis affects the diaphragmatic surface of the lungs, the diaphragm may be penetrated and the disease spread to the liver, peritoneum, and abdominal organs.

Pathologic Histology.—Microscopic sections of tissues from actinomycoses show nodes of granulation tissue, healthy, suppurating or cicatrizing, with the centrally situated characteristic ray-fungi. The disease is commonly suppurative in character, but in the form known as "*wooden tongue*" the chief characteristic is the formation of embryonal connective tissue, by which nodular induration takes place. Secondary infections soon take place in the lesions and greatly accelerate their spread.

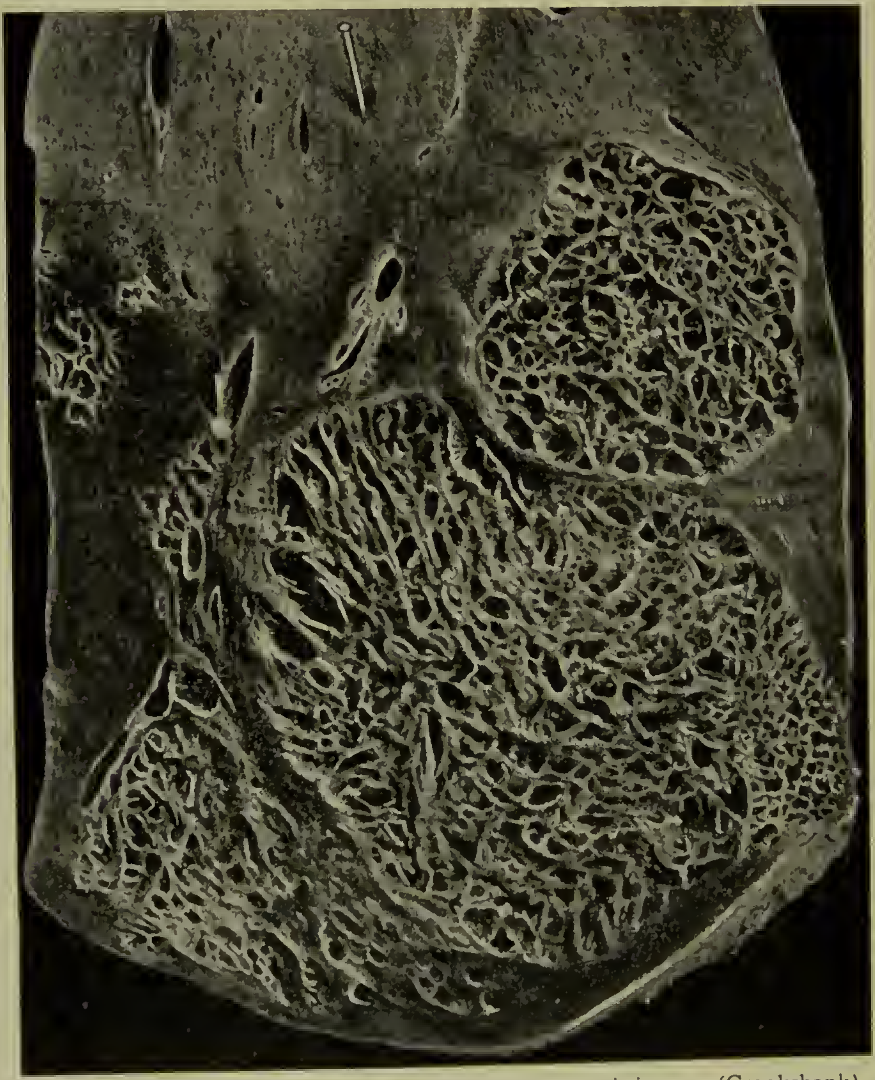

FIG. 216.—Section of liver from a case of actinomycosis in man (Crookshank).

From the jaw and the tongue the disease spreads to the cervical lymphatic glands and thence to the skin of the neck and foreleg. The lymphatic glands of the interior of the neck also become affected, and the disease later extends to the mediastina and to the lungs. From the lungs it may invade the abdomen through the diaphragm, affecting the peritoneum and abdominal organs. Death may occur from a variety of causes—exhaustion, pneumonia, peritonitis, etc.

In a case of primary actinomycosis of the intestine seen by Chiari, the formation of inflamed plaques with a whitish mycelial covering took place, while a case observed by Zemaan was characterized by nodular mucous and submucous formations which contained the specific fungi and disintegrated to form ulcers. The intestinal disease spreads to the peritoneum and other abdominal viscera.

Except when very radical excision of the diseased tissue can be effected, the disease is commonly fatal.

Mycetoma (Madura foot; pied de Madura; fungus foot of India) is a chronic, specific, infectious, inflammatory affection caused by the Actinomyces maduræ, discovered by Vincent in 1894. This peculiar disease of the feet is often encountered among the agricultural classes of the Indian provinces. When first investigated, it was thought to be closely related to actinomycosis, because of the presence in the pus discharged from the lesions of certain pinkish or blackish bodies of minute size and rounded form, similar to the actinomyces fungus. When subjected to careful investigation by Vincent, it was shown, however, to be a somewhat different affection, caused by a fungus now known as the Actinomyces maduræ. The disease is known to have a wider distribution than was originally supposed, isolated cases being seen elsewhere than in tropical India, one or two having been observed in North America. It is also known not to be exclusively a disease of the foot, as was at first supposed, but to affect other portions of the body, as the leg, the hand, the arm, the shoulder, and the hip. As usually seen, it begins in one of the fleshy pads of the great toe. The patients commonly attribute the onset of the disease to the prick of a thorn, and if this theory be correct, it is small wonder that the disease is more common in the foot than elsewhere, as the native population of India go barefoot in a country abounding in thorns.

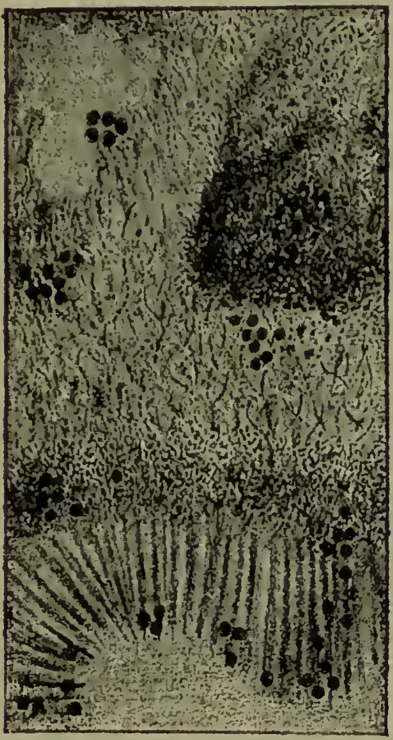
FIG. 217.—Actinomyces maduræ in a section of diseased tissue (Vincent).

For several weeks following the injury no symptoms are observed; then the affected pad begins to swell, forming a nodular enlargement which eventually becomes the size of a marble. The suprajacent skin becomes purplish in color, thickened, indurated, and adherent. For a long time the progress of the disease is slow; months pass without much perceptible change. Secondary nodes in other parts of the foot may gradually develop; after a year or two the nodes soften, suppurate, and discharge a thin pus, in which are found the small spheric bodies already described. The bodies are usually pinkish in color and are compared to "salmon roe" in appearance. Sometimes they are black and are said to resemble grains of gunpowder. Two forms—the *pale* and the *melanoid*—are, therefore, described. As the disease progresses and other nodes soften, additional external openings are formed, between which internal communicating sinuses form. As time passes the formation of nodes continues, until the foot is distorted into an almost shapeless mass of enormous size (the foot is said to resemble a ham), full of suppurating sinuses, the skin upon the surface having a rather velvety appearance. Curiously enough, the disease is painless, so that the afflicted individual continues to walk about on the grotesquely deformed extremity. Death may ultimately result from asthenia, but only in rare instances.

Bacteriology.—The organism which Vincent succeeded in isolating is a form of actinomyces. The "grains" found in the pus and the clumps which form in artificial media consist of masses of tangled branched filaments. The clubs which characterize Actinomyces bovis are absent. Spores occur in many of the threads.

The organism stains well by ordinary staining solutions and by Gram's method.

Cultivation.—It can be cultivated artificially, Vincent finding that acid vegetable infusions were particularly well adapted to the purpose. It grows in the usual laboratory media. In bouillon, both at 20° and at 37° C., in four or five days, minute spheric colonies, which in about three weeks become as large as a pea, make their appearance. The colonies usually cling to the glass, and those which develop at the surface of the fluid present a rose color.

Cultures in gelatin are not luxuriant, are colorless, and cause no liquefaction.

Upon agar, strikingly beautiful, rounded, glazed colonies form, at first colorless, but later rose-colored or bright red. Most of them remain isolated, attaining the size of a small pea. They are usually umbilicated, like a small-pox pustule, and present a peculiar appearance when the center is pale and the periphery red. As the colony ages, the reddish color disappears and it becomes dull white. The colonies adhere closely to the medium upon which they grow, and are of almost cartilaginous consistence. The organism grows in milk, but causes no coagulation. Upon potato the growth is meager and the red color faint, although more marked if the reaction of the potato be acid.

Pathogenesis.—Vincent was unable to reproduce the disease by the introduction of the fungus into the lower animals.

Wright found that the *melanoid* form depended upon a higher fungus belonging to the moulds.

Morbid Anatomy.—The healthy tissue is said to be sharply circumscribed, the diseased masses appearing as large degenerated nodes except when vascular. In these nodes the characteristic fungi can be defined by proper methods of staining. They usually occupy a central position, the long filaments, which can be beautifully stained by Gram's method, extending among the round-cells which make up the node. Giant-cell formation is unusual, the lesion consisting almost exclusively of a round-cell infiltration which generally undergoes a speedy coagulation necrosis. Small interstitial and external hemorrhages are very common, occurring from the ulcers and sinuses of the diseased tissue, probably from the abundant newly formed blood vessels.

Farcin du bœuf, or cattle farcy, is an acute, infectious, contagious, inflammatory, and degenerative disease of cattle, chiefly observed in Guadeloupe, caused by the Actinomyces farcinica, and characterized by lymphangitis, lymphadenitis, and pseudotuberculosis of the internal organs.

Etiology.—The disease is caused by the Actinomyces (Nocardia) farcinica, a micro-organism which occurs in the nodes and in artificial culture media in the form of long, delicate, branched threads intricately interwoven. Spores form in large numbers upon the surfaces of old cultures.

The organism stains well by the usual methods, and especially well by Gram's method.

Cultivation.—The organism grows well in artificial media if permitted free access of oxygen. It grows both at the room-temperature and in the incubator at 37° C.

In bouillon it forms colorless masses, irregular in size and shape, some of which float upon the surface, others sinking to the bottom. The surface may be covered with a delicate scum.

Upon agar the growth occurs in the form of small, discrete, irregular, rounded, opaque, dry masses of a yellowish-white color. The general appearance resembles that of cultures of the tubercle bacillus. On potato, pale-yellow, dryish scales rapidly develop. The growth upon blood serum resembles that upon agar. It grows in milk without altering the reaction.

Pathogenesis.—Nocard found that the organism retained its virulence upon artificial media for a long time, even after it had been kept for four months in an incubating oven at 40° C.

The organism is pathogenic for guinea-pigs, cattle, sheep, dogs, rabbits, etc. Horses and asses are immune. The disease is not known to affect man.

Experimental inoculation into guinea-pigs is followed by the formation of a voluminous abscess at the seat of inoculation, followed, after evacuation, by lymphangitis and lymphadenitis, secondary suppurations with phlegmon formation, extreme prostration for a time, but subsequent recovery.

Intraperitoneal and intravenous inoculations in guinea-pigs and rabbits are followed by a form of the disease resembling tuberculosis.

Pathologic Histology.—Microscopically, the disease resembles tuberculosis; the small nodes found in the internal organs consisting centrally of a mass of disintegrated, degenerated cellular remnants, in which are massed the tangled threads. Surrounding this is a zone of round-cell infiltration, beyond which an attempt at organization can be observed.

Morbid Anatomy.—The early lesions appear in the skin, chiefly of the neck, with the formation of small nodes which soon soften and suppurate. The lymphatic vessels and cervical glands are soon affected, the disease spreading to the axillary, tracheal, and prescapular glands, and finally to the lungs.

The affected glands first enlarge, from the presence of the nodes, then soften, suppurate, and evacuate.

To the naked eye the lesions of the internal organs closely resemble tubercles. When the cultures are injected into the peritoneum, it is said that the pseudotubercles which form affect the peritoneum only, and not the organs beneath it.

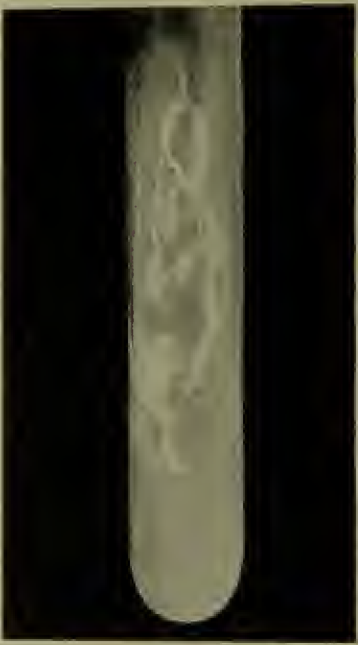

FIG. 218.—Streptothrix of farcin du bœuf growing on glycerin-agar.

Rhinoscleroma is a chronic, infectious, inflammatory, and productive disease of the skin and mucous membranes of the nasal passages, probably caused by the Bacillus rhinoscleromatis, and characterized by the formation of small, firm nodules. The disease is of infrequent occurrence. It is described chiefly by German authors, and is better known and more frequently seen on the Continent of Europe than elsewhere. It usually begins upon the face, at the junction of the nostril and the cheek, or upon the ala nasi, and is characterized by the formation of rather small, hard nodes, which project from the surface as hard, smooth papules. These develop upon the nose, both externally and internally, and, by extending through the anterior nares, the disease may reach the posterior nares, or it may descend upon the lip and then extend to the mucous membrane of the mouth, or reach the hard palate by extension from the posterior nares. The number and size of the nodes may almost completely occlude the nares. From the nose and lip the disease sometimes descends upon the jaw. It, therefore, causes considerable disfigurement and no little inconvenience to the patient. The lesions are never associated with ulceration, but consist entirely of semidiscrete nodes, composed of granulation tissue whose tendency is toward organization rather than necrosis. Because of the enlargement and disfigurement, the disease is described as "Pfundnase," or pound nose, by the Germans.

Etiology.—The disease is so constantly associated with the presence of Bacillus rhinoscleromatis of von Frisch that it is now accepted as its cause.

The organism is a short rod with rounded ends, and is surrounded by a distinct capsule. It closely resembles in morphology and vegetation upon artificial culture media Bacillus pneumoniæ of Friedländer (*q. v.*), the points of difference being that the Bacillus rhinoscleromatis stains by Gram's method, and does not lose its capsule when artificially cultivated.

The pathogenesis of the organism is about the same as that of Friedländer's bacillus. All experimental inoculations have thus far failed to produce anything resembling the disease in animals.

Pathologic Histology.—Histologically, the lesion consists of a dense, cellular infiltration of the corium and papillary layer of the skin. From these cells new connective tissue seems to be formed, so that organization is always a part of the process. The majority of the cells undergo a peculiar hyaline degeneration. The cells are frequently vacuolated. The nodes are quite rich in lymphatic vessels. The bacilli are found scattered through the nodes, and are frequently inclosed in the cells, which then nearly always show the hyaline degeneration.

The disease is occasionally seen in the throat, the gums, the larynx, and rarely in the trachea. In the throat and respiratory organs it sometimes forms dense cartilaginous swellings, sometimes contracting connective tissue. When incised, the infiltrated tissue appears yellowish, sometimes showing a grayish or gray-red color.

The disease does not destroy life. It is essentially chronic in nature, is without acute inflammatory symptoms, is not destructive in the sense of ulcerating or eroding the tissue, and does not distribute to the internal organs.

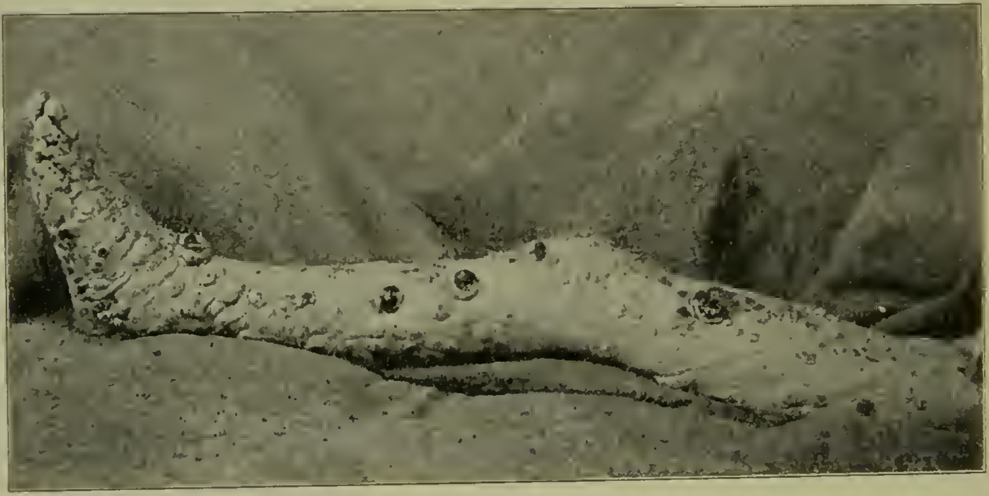

FIG. 219.—Granuloma fungoides of thirteen years' duration in a male aged forty-seven (Stelwagon).

Mycosis fungoides, or granuloma fungoides, is a peculiar, probably inflammatory, disease of the skin and mucous membranes. It is of rare occurrence and unknown etiology, and it is characterized in its inception by a variety of mild disorders of the skin, such as erythema, urticaria, eczema, etc., followed by the formation of a node in the subcutaneous or submucous tissue. This node increases in size, has a distinct red color, is rather hard, and may be painful. As the lesion advances softening usually occurs, followed by extensive ulceration, by which a subcutaneous or subepithelial mass of granulation tissue, dark red in color and sensitive to the touch, is brought to view. The appearance has been compared to a tomato. Usually there is no attempt at healing, but the lesion progressively increases in size, the superficial ulceration continuously discharging pus from its surface. The scalp, face, and upper extremities seem to be most frequently affected. There may be a single lesion, or there may be several, showing different ages and different stages of development.

The lesions may become as large as a hen's egg or a small apple. The patients usually die of exhaustion.

Microscopically, the entire mass of tissue is composed of what appears to be granulation tissue, composed of small round-cells, epithelioid cells, and occasional small giant-cells. Connective-tissue fibers are seen traversing the growth, sometimes singly and sometimes in bands. The growths are imperfectly vascularized, the blood vessels being of new formation. The irregular distribution of the blood probably explains why softening and ulceration so commonly occur. The cause of the disease has not yet been discovered. Micro-organisms, both bacteria and protozoa, have been described, but as yet the etiology of the disease is unknown.

Some believe that the lesion is a superficial form of sarcoma, and while it is true that sarcoma and granulation tissue are with difficulty differentiated from each other by the microscopic appearances, the superficial nature of the lesion, its central softening and ulceration, its slight tendency to heal, its vascularity, its progressive course, and its indisposition to give metastasis would seem to indicate that it is properly classified among the specific infectious diseases.

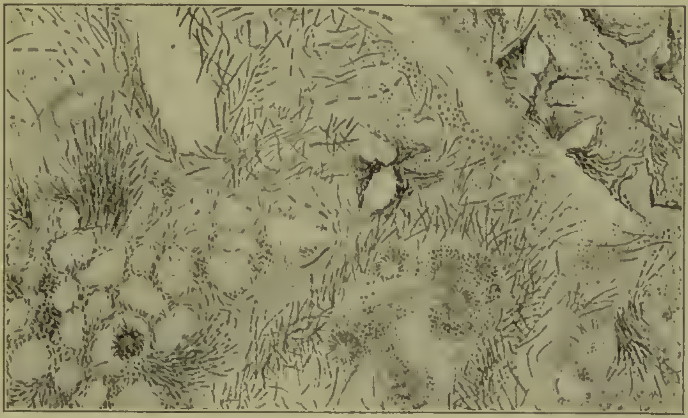

FIG. 220.—Section of bovine lung from a case of pneumomycosis aspergillina, showing the aspergillus fungi in the tissue (Ravenel).

Others regard the disease as analogous to leukemia and Hodgkin's disease, and have described it as *pseudoleukemia cutis*. The chief argument in favor of this view is that in nearly all cases there is an accompanying enlargement of the lymphatic nodes, especially in the neighborhood of the dermal lesions. This might be accounted for, however, by infection, etc., occurring in the primitive lesion.

Mycosis aspergillina is a rare form of pseudotuberculosis, occurring in man and cattle, caused by the aspergillus.

Etiology.—It is caused by some species of aspergillus, probably in all cases Aspergillus fumigatus, which, having been inhaled into some particularly favorable nidus of the pulmonary tissue, has succeeded in adopting a parasitic existence with the formation of inflammatory nodular lesions. The characteristics of the fungus have already been given.

Morbid Anatomy.—The diseased organs show a superficial resemblance to tuberculosis. Scattered throughout the affected organs are more or less numerous, irregular sized, consolidated, bronchopneumonic areas, which show a softened, purulent center and an infiltrated border. There is no characteristic by which the nature of the affection can positively be determined with the naked eye.

The aspergillus can be cultivated from the lesions, and upon microscopic examination of sections of the tissue the mycelial threads of the fungus are seen to form a tangled, thready mass radiating in all directions from the center. Should the node be necrotic, the fungus sometimes dies in the center and then appears as a kind of wreath about its periphery.

Spores of the fungus suspended in fluid and injected into the ear vein of a rabbit may lead to a generalized mycotic infection resembling the spontaneous disease.

Chancroid.—The *chancroid*, *soft chancre*, "*simple sore*," *non-specific sore*, etc., is a specific infectious disease, characterized by an ulceration, usually seated upon the organs of generation, followed by the formation of an inguinal bubo prone to suppuration. The disease is not followed by constitutional symptoms and tends toward recovery.

Etiology.—The disease is contagious, and is usually acquired through sexual contact. It is now fairly certain that the bacillus of Ducrey is the specific micro-organism of chancroid, though staphylococci, streptococci, gonococci, etc., are found in the lesions. The bacillus can be demonstrated without difficulty by staining the secretions with methylene-blue and quickly decolorizing with weak acetic acid. The bacillus is diplococcoid, measures about 0.5 by 1.8, is constricted at the center, stains most deeply at the poles, and sometimes occurs in chains. It is thought by Ducrey, Unna, and others to be the specific organism of the disease. Its cultivation has only recently been achieved.

While the chancre is usually single and indurated, the chancroid is commonly multiple, soft, moist, and pus-discharging. At times the lesion spreads rapidly, undermines the tissues, and assumes a *serpiginous* character; at other times it becomes *phagedenic*. The formation of the bubos is rapid, and the enlarged inguinal glands soften, suppurate, and evacuate, with the formation of communicating sinuses. Less prominent cicatrices form than succeed syphilitic lesions. This disease is purely local, and when uncomplicated, is never followed by constitutional manifestations. In some cases difficulty of diagnosis and prognosis results from the fact that chancre and chancroid may co-exist.

Syphilis.—*Syphilis*, or "*lues*," is a specific, infectious, highly contagious, acquired or hereditary disease, usually, though not necessarily, disseminated through sexual contact, characterized by a chronic course whose manifestations are described as primary, secondary, and tertiary.

Keen and White, who closely follow Cornil in writing upon the subject, divide the course of the disease as follows:

1. Period of primary incubation, lasting about three weeks.
2. Period of primary symptoms—chancre and adenitis.
3. Period of secondary incubation, lasting about six weeks.
4. Period of secondary symptoms, lasting from one to three years.
5. Intermediate period of two to four years, during which the disease may recover.
6. Tertiary symptoms of unlimited duration.

1. The Period of Primary Incubation.—The disease, as has been said, usually results from impure sexual contact. During the period of primary incubation there are no symptoms, so that the third week is usually reached before the *primary lesion—the chancre*—makes its appearance. The chancre first appears as a superficial papule which gradually increases in size, both in circumference and depth, for a number of days. This lesion always forms at the seat of inoculation. Ordinarily it is a single lesion, although multiple chancres are occasionally seen. It never repeats itself, occurs nowhere except at the seat of original inoculation, and is invariably present except in congenital syphilis and in a few cases in which inoculation has been experimentally made directly from the blood into the blood of a susceptible person.

The chancre results from the local development of the germ of disease at the point of inoculation. From the time the chancre begins to form, the spread of the disease begins by lymphatic invasion, and by the time the chancre is well developed, metastatic enlargement of the neighboring lymphatic glands can be observed. The glands thus enlarged are hard, free of inflammatory symptoms, painless upon pressure, and movable beneath the skin. They do not suppurate. Chancres are *genital* or *extragenital*, according to position. The great majority are genital because the disease is usually implanted by sexual contact, but the transfer of the virus to other parts of the body by the finger, by implements, by tattooing, etc., may be followed by extragenital implantations and extragenital chancres.

Genital chancres are most frequent upon the glans penis, the inner surface of the prepuce, and especially upon the fossa glandis and frenum. They may also occur upon the skin of the penis, at the meatus urinarius, upon the scrotum, in the urethra, and upon the groin; in women, upon the labia majora, the clitoris, the skin of the pubes and groin, and the neck of the uterus.

Extragenital chancres occur about the anus in one of the puckers caused by contraction of the sphincter muscle, the mouth, lips, tongue, uvula, palatine arches, tonsils, cheek, nipple, eyelid, finger, etc. Wherever the primary sore makes its appearance, there the lymphatic invasion of the disease begins, so that while in genital chancre it is the inguinal glands that first enlarge and form the bubos, in cephalic chancres it is the cervical glands, and in digital chancres, the epitrochlear and axillary glands.

2. *The Period of Secondary Invasion with the Enlargement of the First Lymphatic Node.*—One by one the disease affects the nodes, in the immediate neighborhood at first, but more and more remote nodes of the body appear to be enlarged, firm, freely movable, and insensitive. During the time of lymphatic invasion the chancre heals, leaving a small, permanent induration.

3. *The period of secondary symptoms* makes its appearance with the lymphatic generalization. The patient now suffers from fever of 100° to 101° F., articular pains, malaise, loss of hair, cutaneous eruptions, and *mucous patches.*

The early cutaneous eruptions are very superficial, and consist of maculæ and roseola; the later eruptions are deeper and form papules and pustules. The eruptions are usually polymorphous, numerous forms of eruption occurring at the same time. The most characteristic feature of the syphilitic lesions is their tendency to adopt an unusual though symmetric distribution. They are frequent upon the palms of the hands, and usually have a rounded form and a copper-red color.

The loss of the hair is incomplete and irregular, affecting the head, eyebrows, mustache, beard, and pubic and axillary regions, so that they present a moth-eaten appearance.

Mucous patches occur upon the skin contiguous to the mucous membranes and upon the membranes themselves. They form slightly elevated, grayish or reddish, glazed, moist, and slimy lesions, covered with a thin pseudomembrane. They are usually observed to occur under the influence of warmth and moisture, and are said to result from the transformation of a syphilitic papule. They occur chiefly upon the prepuce and glans penis, the scrotum, and anus of men, and upon the labia and anus of women. They also occur about the lips, under the tongue, and in other parts of the mouth. They are probably the most contagious of the syphilitic lesions.

The period of secondary symptoms is from one to three years in duration. As the time passes, the manifestations gradually subside, until health is apparently regained.

4. The Intermediate Period.—The patient now passes into what is described as the intermediate period. He may recover with the disappearance of the secondary symptoms, and show no further signs of disease, but in less favorable cases the disease reappears after from two to four years with what are known as *tertiary symptoms.*

5. The tertiary period is of unknown duration. Its lesions are extremely destructive, the most characteristic being the *gumma.* The tendency of the tertiary lesions is to occur in and destroy the deeper organs and tissues. They are always necrotic or ulcerative, and occasion extensive loss of substance, with great subsequent cicatrization.

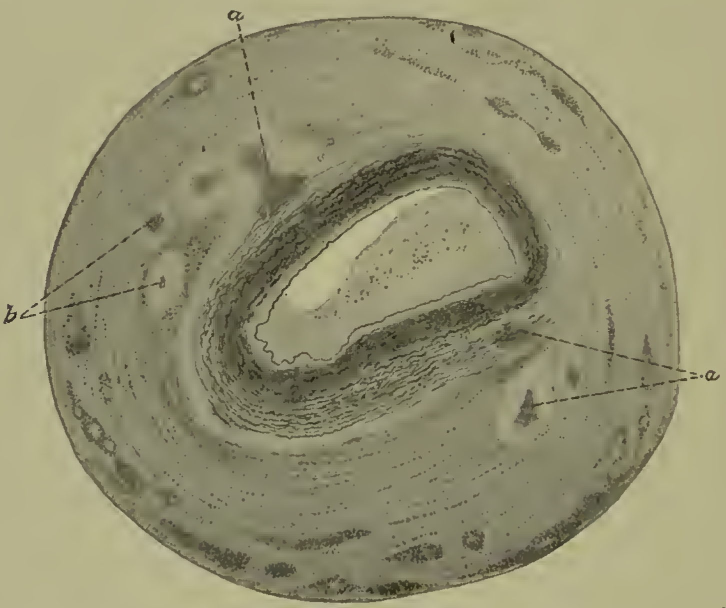

FIG. 221.—Syphilitic arteritis. The section is from a subclavian artery nearly obliterated by proliferation of the intima. The elastic fibers of the intima are greatly increased in number. The media is studded with numerous small gummata (*a*, *a*), in some of which giant-cells (*b*) are present. The adventitia shows some round-cell infiltration (Dürek).

The tertiary manifestations are extremely irregular, both as regards their distribution and their time of occurrence. Sometimes twenty and even thirty years elapse between the development of the primary lesion and the appearance of the tertiary manifestations; the later the lesions are deferred, the more severe and destructive they are apt to be. Not only do very destructive dermal lesions—rupia, etc.—and gummata make their appearance during the tertiary stage, but also less clearly marked lesions of the bones,—osteoperiostitis, rarefying osteoperiostitis, osteomyelitis, and gummatous osteoperiostitis,—of the muscles,—myositis and succeeding contractures,—and of the nervous system—sclerosis of the posterior columns of the spinal cord, etc.—make their appearance. Throughout the course of the disease the blood vessels are prone to show marked changes whenever near a lesion of the disease, and syphilis is an important cause of arteriosclerosis with resulting aneurysm, apoplexy, thrombosis, etc.

Contagion in Syphilis.—The chancre is an infective lesion, though it is improbable that syphilis is frequently transmitted by its secretions. The greatest danger occurs in the secondary stage of the disease, when its course is actively operating in the blood and occasioning superficial manifestations, such as the mucous patch, which is probably the chief contagious lesion.

During the secondary stage the blood is also infectious, and it is possible to transmit the disease by a blood-to-blood inoculation without producing the primary manifestations. Hereditary transmission of syphilis occurs during the secondary stage.

After the lapse of four or more years, while the disease may not cease its manifestations in the infected individual, it ceases to be transmissible, and during the tertiary stage it is universally conceded that it is *not* contagious.

Hereditary syphilis, which begins with the secondary manifestations, is as contagious as the acquired form of the disease.

Etiology.—The cause of syphilis is unknown. Its course and manifestations are, however, so fully in accord with the facts and phenomena of infection as to leave no doubt but that it depends upon a parasitic micro-organism.

From time to time different investigators have described bacilli, protozoa, etc., for which etiologic importance has been claimed, but the bacillus of Lustgarten, which once claimed attention, was subsequently proved to be the smegma bacillus; the bacillus of Van Niessen has received no confirmation, and the protozoön of Schüller is too new to merit more than mention.

Morbid Anatomy.—The lesions peculiar to syphilis are the *chancre*, the *mucous patch*, and the *gumma*. About the cellular infiltrations, arteritis, and fibrosis there is nothing characteristic.

1. The Chancre.—The chancre is the primary lesion of acquired syphilis. It invariably occurs at the seat of primary inoculation, and only in rare cases, in which the inoculation is made into the blood, has syphilis been known to occur without this lesion. It does not occur in hereditary syphilis because it is a blood inoculation.

The chancre of syphilis is the true, hard, or Hunterian chancre. The soft chancre, or *chancroid*, is an entirely different disease (*q. v.*).

The chancre first makes it appearance as a soft red papule which slowly enlarges by superficial and deep infiltration of the tissues until it attains a diameter varying from a few millimeters to several centimeters. It undergoes early superficial necrosis, the resulting ulceration being indolent. Its appearance is suggestive, but not characteristic. It has a dull red color, forms a flattened swelling the ulcerated surface of which is covered with a grayish or yellowish false membrane, and appears either dry or slimy. The induration which accompanies the lesion is quite extensive and very characteristic—hence its name, *initial sclerosis*.

"The induration may be either superficial or deep, depending upon the arrangement of the vessels, which form on the skin two horizontal networks—one beneath the papillæ, the other deeper, at the base of the derma. When the former is affected, we have a superficial induration. If the sclerosis has involved at the same time both sets of vessels, the intermediate branches being equally affected, we have a more extensive nodule, varying in thickness according to the region of the skin involved."

The induration of the chancre is present by the end of the first week of its existence, although sometimes it does not appear until later. It begins at the surface and descends. According to its thickness and the impressions it imparts to the palpating fingers, it is described by syphilographers as a "*laminated induration*," when suggestive of a piece of paper; a "*parchment-like induration*," when somewhat thicker; a "*nodular induration*," when thick and rounded like a piece of wood or cartilage beneath the surface, or an "*annular induration*" when the edges are indurated, forming a hard ring about an ulcer the center of which remains soft.

The chancre having attained its maximum size in a week or two, remains indolent and stationary for three or four weeks, then slowly disappears, recovering entirely in five or six weeks. The induration may, however, persist for years subsequently.

The abrasion through which the initial introduction of the virus takes place may serve as the portal through which other infectious agents simultaneously enter the tissues; and the necrotic surface of the chancre forms an excellent nidus for the growth of bacteria, so that all chancres do not run the typical course, some being modified by associated infections. A frequent result is simultaneous infection of chancre and chancroid, the latter masking the former, so that it may be overlooked, and the simultaneous occurrence of phagedenic inflammations which cause rapid spread of the chancre and obscure its characteristics.

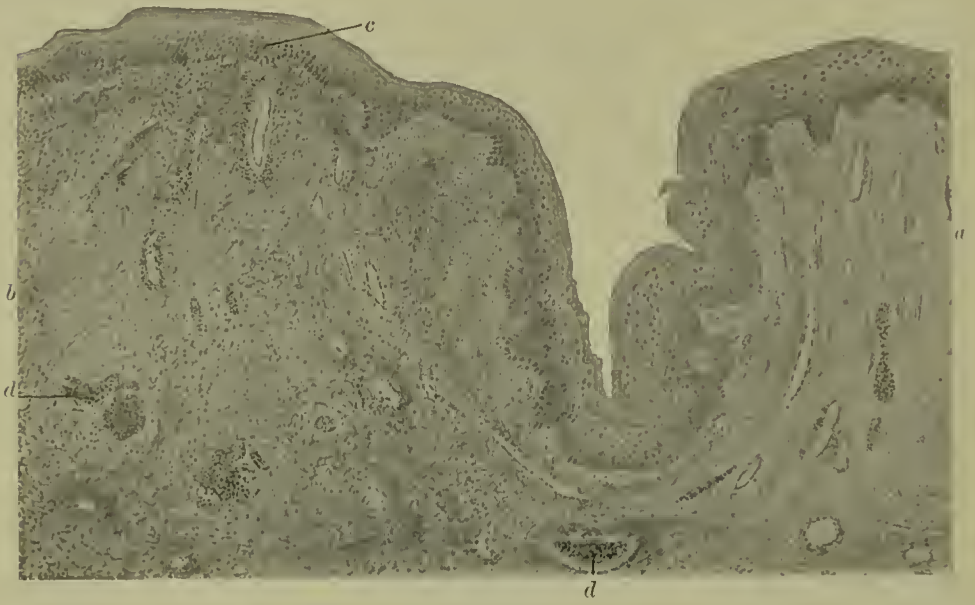

FIG. 222.—Chancre or initial sclerosis of syphilis: *a*, Corium, showing mild inflammation; *b*, chancre, with dense cellular infiltration of the connective tissue; *c*, *d*, lymph-spaces filled with leukocytes (Ziegler).

The chancre is an inflammatory lesion. It is not characteristic in structure, and cannot with certainty be differentiated from other inflammatory lesions by microscopic examination.

It consists of an invasion of the tissue by infiltrating round-cells, which, while indefinite in arrangement, show a general tendency to extend along the course of blood vessels. These cells are polymorphonuclear leukocytes, lymphocytes, and plasma cells, together with endothelial cells, connective-tissue cells, and fibroblasts derived from the tissues. The number of the latter cells indicates considerable disturbance of the connective tissue. There are no giant-cells or peculiar large cells, such as are present in tuberculosis and lepra, to serve as landmarks of the process. The blood vessels in and about the lesion show a peculiar form of arteritis, followed by proliferation of the endothelium, obstruction, and obliteration. The loss of nourishment which follows this vascular change is probably an important cause of the necrotic changes.

There is considerable intercellular exudate, which coagulates in the superficial part of the lesion. The exudate may itself aid in producing the induration—its coagulation certainly does so. The coagulation of the exudate about the cells hastens their coagulation necrosis, the superficial cells entering into the formation of the false membrane upon the surface of the chancre; the deep cells probably also suffer from the coagulation of the exudate among them, although this is not demonstrable. The deep cells are partly absorbed, partly involved, in the connective-tissue hyperplasia which follows.

Although to the eye and finger the chancre seems to be a perfectly circumscribed lesion, the microscope shows its circumscription to be quite indefinite, as cellular infiltrations extend from it in all directions. It is by such extension that the disease reaches the inguinal glands, to form the bubos.

2. *The Mucous Patch or Condyloma Latum.*—These lesions, which are characteristic of syphilis, usually appear in the second stage of the disease, and consist of flat, tabular swellings, making their appearance upon such parts of the skin and mucous membranes as are naturally warm and moist. They begin with the formation of papules which broaden and soften upon the surface from the combined effects of necrosis and moisture. There thus results a lesion, grayish upon the mucous membranes and reddish upon the skin, smooth, moist, and glazed, and covered with a scanty secretion which may be offensive. The lesions are sensitive to the touch.

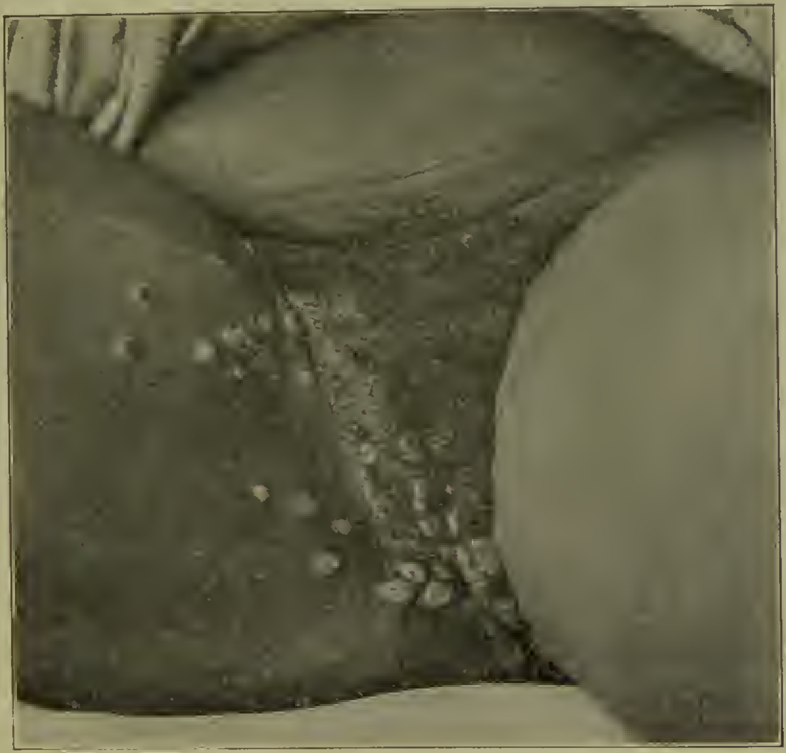

FIG. 223.—Condyloma lata or mucous patches of secondary syphilis (Schamberg).

The mucous patch is the most contagious lesion of syphilis, and as it makes its appearance about the genital organs, is probably that through which the disease is most frequently transmitted. As these patches also occur about the mouth, they may be the source of extragenital chancres through osculation or the use of forks, spoons, etc., used by syphilitics.

The mucous patch consists of a round-cell infiltration of the derma, with edema and necrosis of the epithelium. The papillæ of the skin become abnormally large and broad from the pressure of the new cells and hyperplasia of the epithelial covering. It is this enlargement of the papillæ that is responsible for the elevation. The necrosis and exfoliation of the epithelium leave a slightly oozing, easily infected surface, which is slow to heal. More or less hyperemia of the papillæ of the skin is present, giving the dermal lesions their red color. The grayish color of the lesion, upon a mucous membrane, depends upon the necrotic slough upon its surface.

Mucous patches may be single or multiple. Their recovery is usually perfect, although for some time indurations may remain where they have been.

3. The Gumma.—The remaining characteristic lesion of syphilis is the gumma. It may, in rare instances, make its appearance during the first year of the disease, but usually not until years later, and may first appear as late as twenty to thirty years after infection.

The usual seats of occurrence are the face (nose and nasal septum), scalp, iris, shoulders, neck, arms, thighs, and legs. They may, however, occur in any part of the body, including the internal organs.

The appearance of a superficial gumma is similar to that of a furuncle, but it extends more deeply into the tissues and is much less inflammatory and usually painless. It gradually increases in size until it attains a diameter of one or two centimeters, then softens slowly, extends to the surface, and evacuates. Each gumma has four stages: (1) Formation; (2) softening; (3) ulceration; (4) cicatrization.

The period of formation is longest. Softening and ulceration are also slow, the evacuation of the softened material taking place through a small rounded opening, through the escape of curdy flakes of necrotic or gummy tissue not in the least like pus. Following the evacuation is a cicatrization which terminates in the formation of a deep and drawn scar which usually has a radiating appearance.

Gummata may be single or multiple. There may be one lesion the size of an orange, or there may be hundreds no larger than a pin-head. They occur in both hereditary and acquired syphilis.

The gumma is a specific inflammatory lesion in which the process of coagulation, with the formation of a gummy material, soon exceeds the rapidity of growth, so that a gumma not yet evacuated presents to the naked eye a fairly well-circumscribed mass of grayish or grayish-yellow, firm, coagulation-necrotic material formed by retrogressive changes in the exudation and tissue into which it has exuded. The forming gumma consists of a fairly typical granulation tissue in which newly formed blood vessels are numerous. As the lesion ages, endarteritis occurs in the vessels and aids in the succeeding necrosis. The degeneration of the gumma is called "gummy." It sometimes resembles mucoid degeneration, but is apparently a mixed form of necrosis. The granulation tissue of which the growing gumma is formed consists of both round-cells and fibroblasts, with occasional small giant-cells. The central cells of the gumma first undergo coagulation necrosis, a distinct zone of growing connective tissue usually circumscribing the mass.

Gummata deeply situated in the internal organs, as in the liver, have no opportunity to heal by evacuation, but do so by absorption, the combined softening and absorption occurring simultaneously with the contraction of the connective tissue, until a large lesion is transformed into a knot of fibrous tissue. The amount of connective tissue formed by the healing process may be considerable, and by its contraction produce marked deformity of the organ. Should the absorption process be very slow or incomplete, calcification usually occurs in the necrotic remnants.

4. *The Atypical Manifestations of Syphilis.*—The organs of syphilitics are usually indurated from *hyperplasia of the interstitial fibroconnective tissue.* This is probably a manifestation of the syphilitic poison, though it must not be forgotten that alcoholism is frequently associated with syphilis and may be responsible for the cirrhosis of the liver and other indurations observed.

Cellular infiltrations beneath the mucous membranes, especially in the larynx, are common in syphilis, and may lead to ulcerations or indurations. In all probability the indurations of the internal organs follow such cellular infiltrations.

Endarteritis is common in syphilis in and about the specific lesions. This form of endarteritis does not, however, differ essentially from others.

Various *skin eruptions* occur in both secondary and tertiary syphilis. A few, because of their distribution, are characteristic, but the majority are with difficulty differentiated from similar non-syphilitic lesions, except the history of the case be taken into account.

Syphilitic *bone diseases* are common. Periostitis, ostitis, and osteomyelitis occur. These lesions have a selection for the upper third of the tibia, the sternum, and the skull. They may become very destructive, especially when affecting the septum nasi or the bones of the cranium. (See Diseases of the Bones.)

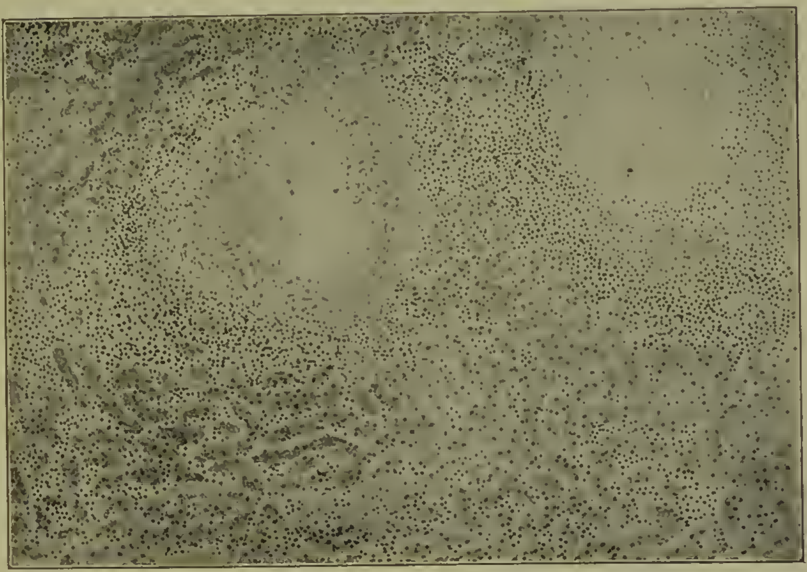

FIG. 224.—Fresh gummatous hepatitis with acquired syphilis (Dürck).

Hereditary Syphilis.—Hereditary syphilis may depend upon disease of the ovum, of the spermatozoön, or of both ; or it may be caused by placental transmission, if contracted by the mother subsequent to conception. It can be inherited from the father only through the medium of the spermatozoön, hence the father of the infected child must be syphilitic at the time of conception. As the mother may infect the child either through a diseased ovum or by blood infection through the placenta, she may either be syphilitic at the time of conception or may contract the disease during pregnancy.

When, as sometimes happens, conception follows the union of a syphilitic spermatozoön and a normal ovum in a woman not infected with syphilis, it is not possible for her to become infected through the placenta from the fetal blood. This immunity of the mother of a syphilitic child is the foundation of "Colles' law" that a syphilitic child born of an apparently healthy mother is incapable of subsequently infecting her. The converse of this is also true, and forms the foundation of "Profeta's law," that an apparently healthy child born of a syphilitic mother cannot be subsequently infected by her.

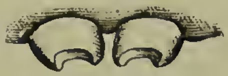

FIG. 225.—Upper median incisors in hereditary syphilis (Cornil and Ranvier).

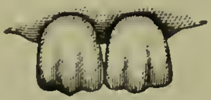

FIG. 226.—Serrations in normal teeth (Cornil and Ranvier).

The transmission of syphilis from parent to child rarely occurs subsequent to the lapse of four years from the time of original infection. Acquired syphilis of the mother may be transmitted to the child *in utero* as late as the seventh month of gestation.

Hereditary syphilis differs from acquired syphilis only in being without the initial lesion. It is contagious, and can be transmitted to others, just as any case of secondary syphilis.

For reasons already made plain, the hereditary form of the disease lacks the primary stage. Instead of virus reaching the child through some external focus where it first forms a chancre, and then invades the lymphatics, the poison, entering from the germinal cells, grows and multiplies simultaneously with the developing embryo, or in case of later infection of the mother, having produced its early manifestations in the body and invaded her blood, passes through the placenta and enters the circulation of the offspring.

Prenatal infection with syphilis is a very serious obstacle to the proper development of the embryo. Exactly how it will interfere with its progress will depend upon the time at which the infection of the embryo occurs and the activity of the disease in the parents. Thus, if the parents suffer from active and malignant secondary syphilis at the time of procreation, the disease in the embryo is usually so active as to cause its death and lead to abortion. The aborted embryo is apt to show exaggerated lesions, such as palmar pemphigus and disease of the internal organs. If the activity of the disease is more mild, the fetus dies later, and is born dead and macerated. It is said that at least one-third of syphilitic children are born dead.

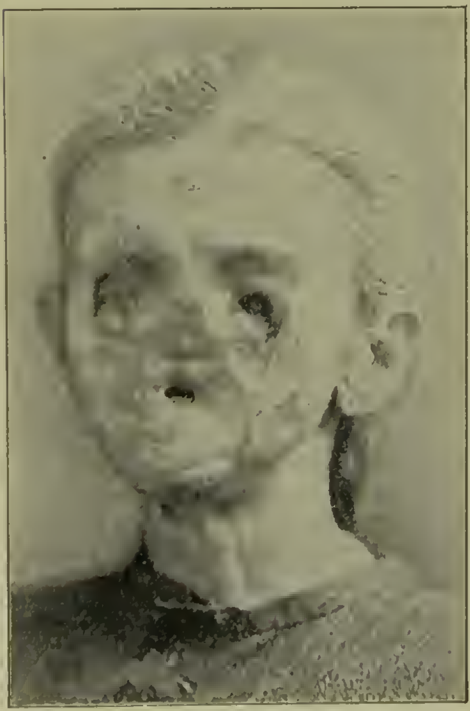

FIG. 227.—Closure of mouth from congenital syphilis (Dandridge).

If the virus is still less virulent, the children may be born alive with evidences of the disease, when they usually die shortly, or without evidences of its presence, to develop the symptoms and fall into an unhealthy condition shortly after.

Of these healthy appearing children, it is said that about 25 per cent. die in the first six months. Even if they survive longer, the dangers are overwhelmingly against the subsequent attainment of health and freedom from deformity.

The newly born child of syphilitic parents usually shows no symptoms of the disease for from one to three weeks. About 30 per cent. show manifestations within a month, 66 per cent. of the remainder within three months.

The appearance of the syphilitic child, whether the syphilis be hereditary or accidentally acquired through contact with mucous patches in the maternal tissues during delivery, is about the same, the effect of the disease being a marked impairment of nutrition and growth.

The child appears small, withered, and weazened. Its features are senile or simian. It has a hoarse cry, and suffers from catarrh of the nasal mucous membrane, which causes the characteristic "snuffles." Cutaneous eruptions are frequent, and changes in the bones and joints are partly characteristic.

If the child lives, its life is apt to be a continued succession of morbid processes—pemphigus, coryza, cirrhosis of the liver, osteochondritis, dactylitis, interstitial keratitis, etc.

All its physiologic processes are disturbed and its structure morbidly modified. Thus, the teeth of the first dentition are irregular in development, opaque, chalky, deficient in enamel, with soft friable dentin, inequality in size, and proneness to decay. The permanent teeth are characterized by a peculiarity of the upper central incisors, known as "Hutchinson's teeth," the fang of each tooth being short, thick, and deeply notched at the edge.

As the child grows, various cellular infiltrations, superficial and deep ulcerations, make their appearance, with corresponding cicatrizations and more or less marked disfigurement and deformity.

PART II.—SPECIAL PATHOLOGY.

CHAPTER I.

THE BLOOD.

GENERAL REMARKS.

THE blood is the circulating, life-sustaining fluid of the body. It receives the products of digestion in an assimilable and utilizable form, and conveys them to the various cellular laboratories for refinement. It carries appropriate nutriment to all the cells of the organism, absorbs effete products from the metabolic tissues, and carries them to the excretory organs. Through the hemoglobin contained in its corpuscles it is the means of tissue respiration, oxygen being absorbed in the lungs and carried to the cells, and the carbon dioxid eliminated by the cells taken back for elimination.

The blood consists of fluid—*liquor sanguinis*—and corpuscles.

Physiologically, blood is divided into the *arterial*, or freshly aërated, bright-red blood, the *venous*, or vitiated dark-blue blood, and the *capillary*, or intermediate blood. For purposes of study the blood is sometimes obtained by opening an arterial or venous vessel, either at the surface or in the organs of the body, but in nearly all cases studies of the blood are made from a drop obtained from a small puncture made in the ball of the finger or tip of the ear, and represents the capillary blood of the peripheral circulation. Whenever statements concerning the structure and composition of the blood are made, it should always be borne in mind that they refer not to the total blood or to the blood in the great vessels, but to this easily accessible blood of the peripheral circulation.

This blood used for study is a dark-red, heavy fluid. It is alkaline in reaction, from the presence of disodic phosphate (Na_2HPO_4) and sodium carbonate ($NaHCO_3$). The alkalinity expressed in terms of sodium hydrate, according to different authors, varies as follows:

Von Jaksch . . .	260 to 300 mg.	per 100 c.c. of blood.
Canard	203 to 276 mg.	
Simon	182 to 218 mg.	

These variations seem to indicate that no reliable method of determining the alkalinity has yet been devised, and it is safe to follow von Limbek, Cabot, and others in saying that it is not correctly known.

For clinical purposes one can determine whether the blood be alkaline or acid, in spite of its red color, by the use of glazed litmus-paper, allowing it to remain in contact with the paper for about one-half minute, then carefully washing it off. In this way the corpuscles which give it the red color will be removed and the paper will show the reaction.

The specific gravity of the blood depends upon the number of corpuscles and their percentage of hemoglobin. In children it varies from 1.054 to 1.052. For women, the specific gravity approximates 1.054; for men. 1.055. It is safe to adopt 1.055 as the normal standard for healthy adults.

A simple method of estimating the specific gravity is that of Hammerschlag. It is done by making a mixture of chloroform and benzol of exactly the same specific gravity as a drop of blood permitted to fall from the punctured finger into it. If the drop of blood tends to sink, chloroform must be added; if it tends to float, benzol must be added. As soon as the drop of blood remains suspended, tending neither to rise nor to sink, the specific gravity of the mixture can be determined with a hydrometer and the reading will apply both to the blood and to the chloroform-benzol mixture. The hydrometer used for the purpose must be specially and correctly graduated for measuring the specific gravity of the chloroform-benzol mixture.

The blood has a characteristic odor, which in different animals resembles the pulmonary exhalations.

It is somewhat difficult to make a correct chemic analysis of blood, because of the rapid formation of fibrin when it is shed. According to C. Schmidt, the following calculation represents the chemic composition with fair accuracy:

In 1000 parts of blood:	Man.	Woman.
Corpuscles	513.00	369.20
Water	349.70	272.60
Hemoglobin and globulins	159.60	120.10
Mineral salts	3.70	3.55
Plasma	486.90	603.80
Water	439.00	552.00
Fibrin	3.90	1.91
Albumins and extractives	39.90	44.79
Mineral salts	4.14	5.07

Hoppe-Seyler and Hammarsten give the composition of horse's plasma as—

Water	908.4	917.6
Solids	91.6	82.4
Total albumins	77.6	69.5
Fibrin	10.1	6.5
Globulin	. .	38.4
Serum-albumin	. .	26.4
Fat	1.2	12.9
Extractives	4.0	12.9
Soluble salts	6.4	12.9
Insoluble salts	1.7	12.9

Simon introduces the following table, showing the marked difference existing in the mineral ingredients between serum and red corpuscles, the latter being relatively rich in potassium salts and phosphorus and poor in sodium salts and chlorin.

	Man.		Woman.	
	Erythrocytes.	Serum.	Erythrocytes.	Serum.
K_2O	1.586	0.153	1.412	0.200
Na_2O	0.241	1.661	0.648	1.916
CaO	. .	. .	. .	. .
MgO	. .	. .	. .	. .
Fe_2O_5	. .	. .	. .	. .
Cl	0.898	1.722	0.362	1.440
P_2O_5	0.695	0.071	0.643	2.202

In addition to the composition given, which may constitute the invariable or slightly variable composition of the blood, there are a number of compounds which occasionally present themselves. Among these may be mentioned fat, varying from 0.01 to 0.015 per cent. after rich meals; soaps, cholesterin, lecithin, dextrose, normally about 0.01 to 0.015 per cent., and sometimes even 0.03 per cent., urea, uric acid, kreatin, kreatinin, carbamic acid, sarcolactic acid, glycogen, hippuric acid, and, under pathologic conditions, xanthin, hypoxanthin, paraxanthin, adenin, guanin, leucin, tyrosin, lactic acid, cellulose, β-oxybutyric acid, acetone, and biliary constituents.

The gaseous interchange that takes place in the lungs and tissues causes venous and arterial blood to differ widely in gaseous ingredients; thus we find:

	Blood.	
	Venous.	Arterial.
Oxygen	21.6	6.8
Carbon dioxid	40.3	48.0
Nitrogen	1.8	1.8

Of the oxygen, only 0.26 per cent. is dissolved in the plasma, all the remainder being in combination with the hemoglobin of the corpuscles. One-tenth of the carbon dioxid is in solution of the plasma, the remainder being in the corpuscles in combination with alkalies and with hemoglobin.

TABLE I.—*The Liquor Sanguinis.*

- LIQUOR SANGUINIS.
  - Constituents normal when present in certain amounts only.
    - Positively demonstrable.
      - Nutritive
        - Serum-albumin.
        - Serum-globulin
          - Fibrinoplastin.
          - Paraglobulin.
        - Sugars.
        - Extractives
          - Fats
            - Olein.
            - Palmitin.
            - Stearin.
          - Soaps.
          - Glycerins.
          - Cholesterin.
      - Coagulative
        - Fibrin factors—fibrinogen.
        - Fibrin ferment—thrombin.
      - Protective
        - Cytolytic amboceptors.
        - Cytolytic complements.
      - Enzymic
        - Proteolytic—trypsin (?).
        - Lipolytic—lipase.
        - Glycolytic—pancreatic ferment.
      - Metabolic
        - Urea antecedents.
        - Uric-acid antecedents.
        - Creatin, etc.
      - Inorganic
        - Chlorids—NaCl, etc.
        - Phosphates—Ca, Mg.
        - Carbonates—Ca.
        - Sulphates.
        - O.
        - CO_2, etc.
    - Negatively demonstrable.
      - Stimulating
        - Internal secretions
          - Pituitary.
          - Thyroid.
          - Adrenals.
          - Sex glands.
          - Corpus luteum.
  - Constituents always abnormal.
    - Positively demonstrable.
      - Toxic
        - Protozoan—malaria, Texas fever, etc.
        - Bacterial
          - Toxophorous.
          - Haptophorous.
        - Metabolic
          - Acetone.
          - Aceto-acetic acid.
          - β-oxybutyric acid.
      - Leukomains
        - Xanthin.
        - Hypoxanthin.
        - Creatin, etc.
      - Protective
        - Agglutinins.
        - Precipitins.
        - Amboceptors.
        - Complements.
        - Antitoxins.
        - Anti-enzymes.
        - Anticomplements.
        - Anti-amboceptors, etc.
      - Disintegrative—Hemoglobin.
      - Absorptive
        - Indol and other ethereal sulphates.
        - Bile-pigments.
        - Bile salts.
      - Therapeutic—Drugs, etc.

1. **The Liquor Sanguinis.**—When obtained by centrifugation or by sedimentation of the corpuscles under conditions which prevent coagulation, the *liquor sanguinis*, or *plasma*, is a clear, transparent, slightly yellowish,

somewhat opalescent, albuminous fluid of faintly alkaline reaction. It has a specific gravity of 1.026 to 1.030. Plasma has a pronounced tendency to spontaneous coagulation, and the coagulation of shed blood depends, not upon the corpuscles, but upon chemic changes in the plasma—*i. e.*, the transformation of certain fibrin factors (fibrinogen ?) into fibrin, through the agency of a ferment active in the presence of calcium salts.

The composition of the plasma varies in different portions of the circulation and at different times. Thus, during the period of digestion, the blood of the portal vein contains more sugar and fat than at other times, and after vigorous exercise the blood going to the kidney contains more urea than that leaving it. The plasma also participates in the gaseous interchanges, that which has recently been in the lungs being relatively rich in oxygen, while that recently in the active organs is relatively rich in carbon dioxid.

In this manner the composition of the blood is extremely complex and is constantly varying to accommodate itself to the conditions of metabolism, secretion, excretion, etc., in different parts of the body.

The necessarily complex composition of the liquor sanguinis will be made clear by a glance at the artificial and hence imperfect tabulation on p. 366.

2. **The Corpuscles.**—Many histologists speak of the blood as a tissue, and of the suspended corpuscles as its cells. While this may be true morphologically, it is doubtfully true physiologically, in that the cells of the blood are not genetic or metabolic. In other tissues the cells are the essential vital units. To their energies the existence of the tissue is to be ascribed, and in the event of injury overtaking it, it is to the same energy of the cells that it is to look for regeneration. The blood corpuscles have no such capabilities; they do not form the blood, but are formed in hematopoietic organs and discharged into it; they do not regenerate the blood, but are simply suspended in it.

Three corpuscles—the erythrocyte, the leukocyte, and the plaque—are described. The first is a non-metabolic disc, solely intended for the absorption and transmission of oxygen; the second is metabolic, and probably undergoes definite metamorphoses during part of its life in the circulating blood. The office and importance of the third cell—the plaque—are as yet undetermined.

PATHOLOGY OF THE BLOOD.

CHANGES IN THE BLOOD MASS.

1. **Plethora.**—Plethora is an increase in the total quantity of blood in the body. According to Foster, the amount of blood in the animal is equal to about one-thirteenth of its weight. It is, however, difficult to estimate, requiring that the body be comminuted, every drop of blood collected and weighed, and then the residual tissues weighed, and the proportion worked out from this. In the absence of any clinical method of determining the total blood in the living body, it is an assumption to conclude that a true plethora ever exists, and the experimental evidences indicate that it is impossible to bring about a permanent increase in the total quantity of blood. An artificial and temporary plethora can be produced in cases of bloodless amputation, in which the blood contained in the limb has been driven into the body by means of an Esmarch bandage and also in the transfusion of blood from one animal to another. In such artificial plethoras it has been determined experimentally that the increase in the amount of blood is only temporary, and not permanent, and the excessive fluid is soon eliminated and the

corpuscles destroyed. The water is excreted in a short time by the urine, and all the excessive or foreign corpuscles disappear in a few days.

There is, however, a certain body-habit, characterized by a rosy hue of the skin, distention of the superficial vessels, and a large heart, usually accompanied by marked deposition of adipose tissue, and followed by disturbances of the renal circulation, in which it seems probable that a greater relative proportion of blood exists than is normal to the individual. The fact that such a "full habit" is apt to occur in "high livers," and especially in beer-drinkers, makes it still more probable that there is an increased quantity of blood in the body. As Stengel points out, however, the apparent superabundance of blood, especially in the case of the beer-drinker, may be due solely to disturbances of the vasomotor system. The full habit is also apt to be a family or personal peculiarity, under which circumstances it can scarcely be called an abnormality.

2. **Oligemia** or **anemia** is the opposite condition, in which the total quantity of blood seems to be less than normal. It occurs temporarily after large hemorrhages, the loss of blood, except when excessive, being readily replaced. It is possibly true that persons of feeble habit have less than the normal or average quantity of blood, but it is impossible to prove it. In the various cachexias and the profound anemias the appearance of the patient suggests a marked diminution in the total blood bulk.

More important, from both the clinical and the pathologic point of view, than the changes of the total quantity of the blood are those observed in its various constituents, especially in the number and kind of its corpuscles and the amount of the coloring-matter they contain.

CHANGES IN THE RELATION OF THE BLOOD CONSTITUENTS.

1. **Oligocythemia** is a diminution in the number of blood corpuscles. It is very common, and forms the chief feature of most of the clinical anemias. It may depend upon considerable or repeated loss of blood, infectious and toxic diseases, lead, mercurial, and other intoxications, wasting diseases, starvation, bad hygiene, insufficient and irregular action of the blood-making organs, and the increased activity of the hemolytic or corpuscle-destroying function.

2. **Polycythemia** is a term used to describe an increase in the number of corpuscles. By others it is restricted to an increase in the erythrocytes, in speaking of which we will refer to it again. Polycythemia, as a relative increase in the total number of corpuscles, may be seen in cholera and in the severe diarrheas, probably in consequence of loss of fluid from the body.

3. **Hydremia**, or dropsy of the blood, occurs when an abnormal quantity of fluid is retained in the blood from insufficient activity in the kidneys and sweat-glands. It may also occur after severe hemorrhage, the result of which is to diminish the total blood mass, which must be made up as rapidly as possible by the withdrawal of fluid from the tissues of the body.

When the blood is so watery that a given quantity of it contains an abnormally diminished quantity of albumin, the condition is described as *hypalbuminosis*. The albumin in the blood may also be affected by increased consumption of albumin or a deficient supply. Such a condition is met with in the chronic digestive disorders, profuse diarrheas, chronic suppuration, prolonged lactation, profuse hemorrhages, kidney disease, etc. It is thought by some to be the starting-point of the essential anemias. In hydremia the amount of hemoglobin in the blood may be diminished from the normal 14 per cent. to 8, 6, or even to 3 per cent. The explanation of this reduction is the oligocythemia.

TABLE II.—*The Blood Corpuscles.*

- CORPUSCLES.
  - Absolutely increased *polycythemia.*
  - Absolutely decreased *oligocythemia.*
    - Erythrocytes measure $7.5\mu = 5,000,000$ per c.mm.
      - Deficient—All forms of anemia.
      - Increased—Rare forms of diarrhea—Polycythemia.
      - Peculiar
        - In size
          - Abnormally small—Microcytes.
          - Abnormally large—Macrocytes and megaloblasts—Pernicious anemia.
        - In structure—Nucleated—Megaloblasts—Pernicious anemia.
        - In shape—Poikilocytes—Pernicious anemia.
        - In color
          - Absolute deficiency of hemoglobin—*Chlorosis.*
          - Absolute increase of hemoglobin—*Pernicious anemia.*
        - In staining—Polychromatophilia.
    - Leukocytes measure 7 to $12\mu = 7500$ per c.mm.
      - Deficient—Leukopenia or Hypoleukocytosis.
      - Increased—Hyperleukocytosis.
        - Cells normal to the blood
          - Polymorphonulear
            - Physiologic.
            - Pathologic—infection, intoxication.
          - Lymphocytes
            - Physiologic.
            - Pathologic—leukemia, lymphatic.
          - Eosinophiles
            - Physiologic—infancy.
            - Pathologic
              - Infection—gonorrhea.
              - Helminthiasis
                - Trichinella.
                - Uncinaria.
              - Sarcoma.
        - Cells abnormal in the blood—Myelocytes—Leukemia, myelogenous.

4. **Anhydremia.**—Concentration of the blood occurs in cholera, severe diarrheas, profuse sweating, and other pathologic conditions associated with marked loss of body fluids. The blood is said to appear thick, and contains an excessive relative quantity of albumin, so that a condition of hyperalbuminosis exists.

5. **Hyperinosis**, an increased amount of fibrin in the blood, is sometimes seen in certain inflammatory diseases, especially croupous pneumonia, rheumatism, and erysipelas.

6. **Hypinosis**, the opposite condition, in which there is a diminution of fibrin in the blood, is rarely seen. Whether or not the refusal to coagulate depends upon the loss of fibrin factors has not yet been settled. In hemophilia the blood refuses to coagulate, hence the profuse hemorrhages following trivial injury. The blood likewise refuses to coagulate properly in asphyxia and in poisoning by sulphureted hydrogen, carbon dioxid, and some venoms.

CHANGES IN THE ERYTHROCYTES.

The erythrocytes, or red blood corpuscles, are small, biconcave discs, measuring from 7.5 to 8 μ in diameter. They are rather larger in the races of the North than in those of the South, and show a slight variation in size in each individual. While appearing red when seen *en masse*, they are in reality of a greenish-amber color. Their substance is extremely elastic; normally they are not viscid; they possess considerable resisting power, so that in spite of being constantly subjected to impacts upon one another and the walls of the vessels through which they circulate, they are able to maintain a definite shape, and in man appear as discs with rounded edges and concave surfaces. The erythrocytes are not permanent cells, but are probably short-lived, and are produced solely for the purpose of carrying oxygen, which forms a loose combination with the hemoglobin, which is their essential constituent. When corpuscles with marked peculiarities, making them easily recognizable, such as those of the birds or reptiles, are introduced into mammals, they remain suspended in the circulation but a few days and then disappear. Experiment shows that the hemolysis which occurs under these conditions depends upon hemolytic substances contained in the blood. The life of the erythrocyte is, in all probability, short.

The origin of the erythrocytes is interesting and important. In the embryo the earliest blood-cells are produced outside of the blood, within the angioblastic cells of the mesodermic tract of the vascular area, where the blood islands of Pander are formed. These cells form a network in which, at certain nodal points, active proliferation of nuclei takes place. Some of the cells thus formed acquire protoplasm and become the endothelial cells lining the vessels. Others become converted into the primary blood corpuscles. The intermediate tissue undergoes liquefaction and forms the primitive plasma of the blood. The earliest blood-cells differ in appearance from the erythrocytes as we know them, and are colorless masses of protoplasm containing nuclei and manifesting ameboid movements. In the course of time the cells gradually acquire the discoidal form and characteristic color. The early blood-cells of the embryo multiply by karyokinesis of the nucleus. This, however, ceases long before birth, at which time very few, if any, nucleated erythrocytes are found.

Neumann thought that during early embryonal life some of the red blood corpuscles developed in the liver. About the fifth month the spleen begins to produce corpuscles, and shortly before birth the bone-marrow is active.

After birth erythrocytes have to be formed to replace those that are constantly worn out and destroyed, as well as to increase in number commensurate with the growth of the individual. The red bone-marrow is the great blood-corpuscle-producing tissue, though corpuscles may be formed in the spleen and elsewhere. Among the more common elements of this tissue one can usually observe cells with a strong resemblance to the embryonal corpuscle, being distinguished from the ordinary marrow cells by the hemoglobin-containing protoplasm, smaller size, and unstable nuclei. These cells are often called erythroblasts, and seem to be transitional stages of the red blood corpuscles. When perfecting their development, the nuclei disappear, and the cytoplasm assumes the usual appearance. Numerous observations seem to indicate that the nucleus is extruded from the cell. Much uncertainty attaches to the source of the erythroblasts; whether or not they are descendants of the red blood corpuscle of the embryo is unknown. There is good authority for believing that erythrocytes are also formed in the spleen. It is also commonly believed that the lymphadenoid structure participates in the production of erythrocytes, and the recent studies of the hemolymph glands by Warthin show that they may participate in corpuscle production. The view that they originate from the blood plaques and leukocytes is untenable. It is important to remember the histogenesis of the erythrocytes in studying the diseases of the blood, because it explains the peculiar appearances of many of the abnormal erythrocytes encountered in the essential anemias.

The destruction of red blood corpuscles no further useful to the economy seems to take place chiefly in the liver. The process is known as hemolysis. Under normal conditions it progresses regularly and attracts no attention. Under certain abnormal conditions, such as extensive burns and poisoning by such substances as potassium chlorate and the mineral acids, it takes place with great rapidity, a vastly abnormal number of corpuscles being destroyed. Many of them break up, others dissolve, and still others become functionless. Examination of the blood soon after the ingestion of nitrobenzol, potassium chlorate, etc., will reveal indications of this rapid destruction of blood corpuscles. In cases which are not fatal the fragments of destroyed corpuscles speedily disappear from the circulation. If the hemolysis persists, oligocythemia necessarily results.

1. **Changes in the Size of the Corpuscles.**—In morbid conditions of the blood it is very common for the red corpuscles to vary in size. It must not be forgotten that under normal conditions the corpuscles of any individual may vary between 5 and 8 μ in diameter. When many corpuscles are unusually small, the condition is sometimes described as *microcythemia*. In pernicious anemia very large corpuscles, described by Hayem as *megalocytes* or *macrocytes*, measuring as much as 10 or 11 μ in diameter, are common.

2. **Changes in the Form of the Corpuscle.**—In pathologic conditions, the red blood corpuscles frequently become irregular and of a pyriform, clavate, cylindric, crescentic, or stellate shape. Such irregular cells have been described as *poikilocytes*, and the condition in which they are found is sometimes spoken of as *poikilocytosis*. Ehrlich is of the opinion that the irregularity in the shape of the corpuscle depends upon the splitting-up of their substance; therefore he prefers to call them *schizocytes*.

Poikilocytosis must be carefully differentiated from *crenation*, which is a very common artefact met with in blood examinations. Crenation is a universal alteration in the appearance of the corpuscles, by which they all appear covered with minute projecting nodules or spines. Poikilocytosis, however, takes place within the vessels and indicates a retrograde condition. Crenation takes place outside the vessel, and indicates that the specimen, having been carelessly prepared for examination, has been acted upon by currents of air by which the plasma has become concentrated and of a specific gravity greater than the delicate corpuscles can bear, so that its surface is thrown into numerous folds or wrinkles. Crenated corpuscles can be prepared at will by immersion in concentrated salt solutions, etc. In crenation all the corpuscles appear equally affected, except possibly at the very beginning of the change, and all look alike. Their appearance is sometimes described as that of an unripe horse-chestnut.

According to Stengel, in the severer forms of anemia the erythrocytes are sometimes ameboid.

3. **Changes in the Nuclei of the Corpuscles.**—The red blood corpuscles of the normal human being contain no nuclei. In very rare cases one occasionally finds a nucleated corpuscle in normal blood, and according to Simon and others, free nuclei undoubtedly originating from nucleated corpuscle can sometimes be found. The nuclei are usually invisible, except when the blood has been stained. Stengel has seen a nucleus escape from a nucleated corpuscle while under microscopic observation. In pathologic conditions, and especially in the essential anemias, however, it is quite characteristic to find numerous nucleated erythrocytes circulating in the blood. Their presence is explained by assuming that they are erythroblasts discharged into the blood before having been properly transformed. There

are three classes of nucleated red blood corpuscles—the *normoblasts,* which occur in large numbers in the bone-marrow of healthy persons, especially after hemorrhage, and are supposed to be young corpuscles whose appearance in the blood indicates a rapid attempt at regeneration; *megaloblasts,* abnormally large corpuscles, measuring from 9 to 14 μ in diameter, and sometimes having degenerated protoplasm containing a single large nucleus, which stains a robin's-egg color with Ehrlich's triacid stain, whose presence seems to indicate loss of the proper regenerative power; and *microblasts,* which are smaller than normal erythrocytes, measuring from 2 to 5 μ in diameter, whose significance is probably the same as that of the megaloblasts. Askanazy has seen a case of bothriocephalus anemia in which the blood contained megaloblasts and no normoblasts. The case is said to have recovered.

4. **Changes in the Staining of the Corpuscles.**—Normal erythrocytes do not stain. When dried and heated, they take the acid stains—*i. e.,* eosin, etc.—and become monochromatophilic. Erythrocytes from the bone-marrow and nucleated erythrocytes from cases of anemia are *polychromatophilic,* and take mixed colors with Ehrlich's stain.

5. **Changes in the Hemoglobin.**—The amount of hemoglobin in the blood is, of course, much reduced when the corpuscles are present in diminished numbers. Normally the blood contains 14 parts in a hundred of hemoglobin. It equals 40 per cent. by weight of the erythrocytes.

(*a*) **Diminution of Hemoglobin (Oligochromemia).**—This condition is common in anemia, and forms the chief characteristic of chlorosis. It may depend upon reduction in the total number of corpuscles, or reduction in the amount of hemoglobin in each corpuscle. When the latter is the case, an experienced observer can often determine the condition by examining the corpuscles microscopically, each corpuscle appearing unusually pale, especially at the center, so that they often resemble rings rather than discs. Occasionally in chlorosis corpuscles will be encountered which seem to be entirely without color. Ponfick has described such cells as *shadow corpuscles.*

(*b*) **The hemoglobin may be dissolved in a plasma—hemoglobinemia.** Solution of the hemoglobin in the plasma is an unusual condition, and seems to depend upon the rapid destruction of the red corpuscles by injurious agencies. It occurs in poisoning by venomous snakes, scorpions, mineral substances, such as potassium chlorate, carbolic acid, pyrogallic acid, naphthol, arsenic, sulphid of antimony, hydrochloric acid, sulphuric acid, antifebrin, antipyrin, phenacetin, sulphonal, tincture of iodin, mushrooms, and vegetables containing poisonous glucosids. It also occurs in infectious fevers, and as a result of the hemolysis following the introduction into the circulation of hemolytic serums. The corpuscles are not always immediately destroyed; sometimes the hemoglobin seems to separate with the formation of droplets or granules in the blood corpuscles. Ehrlich has seen cases in which the hemoglobin was condensed within the corpuscle and gave it a coarsely granular appearance. This is sometimes seen in poisoning by phenylhydrazin and other hemolytic substances. Hemoglobinemia is almost always associated with or followed by hemoglobinuria, the kidney being the organ by which the hemoglobin is excreted. Hemoglobinemia also occurs in scarlatina, malaria (black-water fever), typhoid, icterus gravis, syphilis, variola hæmorrhagica, scurvy, extensive burns, frost-bite, and insolation. There are also paroxysmal attacks of hemoglobinemia which follow exposure to cold, etc., in predisposed individuals.

(*c*) **Changes in the Composition of Hemoglobin.**—The hemoglobin is not a stable compound, but one that is continually changing from oxyhemoglobin to reduced or simple hemoglobin, to carbon dioxid hemoglobin, etc. The most common change that takes place pathologically is the formation of undesirable compounds with various substances accidentally introduced into the blood. Thus, in cases of asphyxia from the assumption of carbonic acid the blood becomes of a dark color from the formation of *carbon dioxid hemoglobin.* In carbon monoxid poisoning the blood is cherry red (*carbon monoxid hemoglobin*); in potassium chlorate poisoning, of a chocolate color (*methemoglobin*); in sewer-gas poisoning it is said that the blood has a black and inky appearance. Hemoglobin occurs in the form of rhombic plates or crystals of a reddish-brown color, and is often found in this form in cases in which hemorrhages have been confined so that the hemoglobin has had time to dissolve out of the corpuscles and undergo crystallization. The addition of acids and alkalies to hemoglobin transforms it into an iron-containing pigment known as *hematin.* This is an amorphous, blackish-brown or bluish-black substance. Hematin, as well as a closely related pigment known as *hematoidin,* is sometimes encountered in old transudates, in the stools after hemorrhage, and after meals rich in meats. It occurs in the urine in poisoning by arsenic, and is found in the blood of animals poisoned with nitrobenzol. Acetic acid and salt solution convert oxyhemoglobin into a chlorin compound of hematin known as *hemin.* This is a brown crystal which usually has the form of elongate plates of rhombic shape. The abstraction of iron from the salts of hemoglobin by the use of strong sulphuric and hydrochloric acids gives origin to a pigment isomeric with bilirubin, known as *hematoporphyrin*. The exact composition of the salts and derivatives of hemoglobin can be determined by the use of the spectroscope.

6. **Changes in the Number of the Erythrocytes.**—The normal number of red corpuscles in a cubic millimeter of blood is 5,000,000 in man, and about 4,500,000 in women. Healthy persons sometimes have as many as 6,000,000. The new-born infant usually has about 6,000,000.

Menstruation, lactation, and childbirth all temporarily diminish the number of red blood corpuscles. As the sexual functions are established at puberty, the number of erythrocytes is temporarily reduced—sometimes in females, as in chlorosis, to a degree that becomes pathologic. The number of erythrocytes also undergoes physiologic variation, becoming increased whenever there is temporary concentration of the blood and diminished in hydremic conditions. Vasomotor conditions may change the number of corpuscles by inducing an interchange between the blood and lymph. During digestion, after taking food, the erythrocytes fall in number while the leukocytes increase. This probably depends upon the fact that considerable liquid is taken with the meal. The concentration of the blood during the fast temporarily increases the number of red corpuscles. During starvation, owing to the impoverished nutrition which interferes with their production, the erythrocytes are usually diminished. The corpuscles are usually diminished from 500,000 to 1,000,000 after violent physical exertion. In the new-born infant for the first few days there are from 6,000,000 to 8,000,000 corpuscles present in the blood. About the third week the number declines to the normal. In the very aged there is apt to be an increase in the number of red corpuscles. In all the anemias the number of erythrocytes is diminished. It may decline to 1,000,000 or less. Simon is of the opinion that when there are fewer than 500,000 corpuscles, recovery is probably out of the question. Quincke has seen a case of pernicious anemia in which, just before death, there were only 143,000 corpuscles in the blood.

Diminution in the number of red corpuscles is usually spoken of as *oligocythemia*, while the opposite condition, with increase in their number, is called *polycythemia*. Polycythemia occurs in the physiologic states already mentioned, and from a few pathologic conditions, all of which are rather unusual. For example, there seems to be a relation between altitude and the number of corpuscles in the blood, as if to compensate for the rarity of the air and provide additional absorbing surface for oxygen. The higher the altitude, the more marked becomes the polycythemia, until, at 14,000 feet, 8,000,000 corpuscles are observed in the blood. Polycythemia is also said to occur from certain poisonings, of which phosphorus may be given as an example.

Regeneration of the Blood.—Animals regenerate blood rapidly. Cabot found that more than 4 per cent. of the blood could be replaced in thirty days. The loss of a considerable quantity of blood has no deleterious effect upon the individual. The influence of frequent, considerable-sized hemorrhages does not produce any anatomic alteration or lead to any permanent anemia.

The horses used for the production of diphtheria antitoxin are frequently bled six or seven liters every week. If a horse weighs 1200 pounds, about 100 pounds by weight consist of blood. Supposing the liter to equal 2 pounds, each bleeding of the size given would represent about one-tenth the total blood possessed by the horse. The horse can stand the loss of blood at this rate for a considerable time, and in my laboratory one horse has been bled no less than eighteen times in twenty-four months, an average of six liters each time, without the development of any chronic anemia and without any apparent diminution of hemoglobin. As would naturally be expected, young, well-nourished individuals regenerate their blood more rapidly than the old or the feeble.

It has already been pointed out that after hemorrhage the rapid withdrawal of fluid from the tissues to replace the lost blood produces a hydremic condition. This thin blood contains less than the normal percentage of hemoglobin, and, of course, fewer erythrocytes than normal.

The next change to be observed is a *hyperleukocytosis* (see below).

In the course of a day or two the regeneration of the erythrocytes begins, and in examining the blood one is apt to find a few poikilocytes, some polychromatophilic cells, and a good many nucleated leukocytes of the variety known as normoblasts. When normoblasts are suddenly introduced into the blood in large numbers, the condition is called a *blood crisis*.

The examination of the blood after hemorrhage is of great clinical importance, giving the following information, as stated by Cabot:

1. Whether or not hemorrhage has taken place; if so, the changes already mentioned in the blood will be observed.

2. The extent of the hemorrhage. Supposing the individual to have been well, the amount of blood lost can be gauged with more or less accuracy by the percentage of hemoglobin found.

3. Whether operation, if necessary, can be performed immediately. Mikulicz has established a rule that when the hemoglobin is below 30 per cent., the patient is too much reduced to endure operation.

4. Whether transfusion is indicated. If shock be due to hemorrhage, transfusion is immediately indicated. If shock be due to cerebral hemorrhage, transfusion will do harm. The blood count, by showing how much blood has been lost, shows transfusion indicated or vice versâ.

5. When the patient has recovered sufficient blood to allow of successful operation.

CHANGES IN THE LEUKOCYTES.

The number of leukocytes present in the blood is slightly variable, averaging about 7500 in a cubic millimeter. According to Hayem, there are 6000. Von Limbeck finds 8000 to 9000. Affanassieu finds them present in the proportion of 1 to 600 of the red, while Muir finds them 1 to 500 of the red. Their number is subject to considerable variation according to a number of physiologic and pathologic conditions. Ordinarily there is one leukocyte to every 650 red corpuscles.

Origin of Leukocytes.—In the embryo the leukocytes appear later than the erythrocytes, probably first appearing as migratory mesodermal elements, which enter the circulation by means of their ameboid movement. Beard's embryologic studies of certain elasmobranchiata (sharks and skates) have led him to believe that the leukocytes are formed by metaplasia of the tonsillar epithelium and that they are really epiblastic derivatives. These embryologic findings have been confirmed, though it is not yet generally conceded that leukocytes as we know them in post-embryonal life are of epithelial and epiblastic origin. In later life there seems to be but little doubt that the corpuscles originate in the adenoid tissues and bone-marrow. According to Piersol, the multiplication of existing leukocytes takes place normally and becomes extremely active under the influence of pathologic stimulation. Virchow has always regarded the multiplication of the connective-tissue cells as an important source of leukocytes. Investigation has shown that the lymph leaving the lymphatic nodes and the blood in the splenic vein contain more leukocytes than the lymph entering the nodes and the blood passing to the spleen. While the majority of the leukocytes of the adult are unquestionably produced by the lymphoid tissues, under pathologic conditions certain forms of leukocytes may also be formed in the bone-marrow.

Varieties of Leukocytes.—Unfortunately, there has not yet been devised any satisfactory method of classifying leukocytes. Ordinarily they are classified according to their morphology; attempts have been made to classify them according to their supposed histogenesis, and Ehrlich has classified them according to the varieties of granules found in their protoplasm.

1. **The Polymorphonuclear Neutrophile or Polynuclear Leukocytes.**—These cells constitute the great majority, and according to most authorities, between 60 and 75 per cent. of the leukocytes. They are somewhat larger than the red blood corpuscles (9 μ), have a

slightly granular cytoplasm in which the appropriate dyes used for staining the blood reveal a large number of small, rounded, neutrophilic granules. The cells are ameboid and phagocytic, and, therefore, of importance in connection with the infectious diseases, in most of which their number is increased. They are also migratory cells, and leave the blood vessels to enter the tissues in acute inflammatory conditions, to make up the great bulk of the pus-cells. The nuclei of the cells are remarkably irregular in shape. Some are lobed and twisted. Many are shaped like the letters S, Z, E. No two cells have nuclei of exactly the same shape. Some appear to have several nuclei, but bridges of nuclear substances can be found connecting them, so that the term polymorphonuclear is more correct than polynuclear. When stained with one of the Ehrlich anilin-dye preparations, the nucleus assumes a deep-blue or greenish-blue color, some portions, which probably contain more chromatin than others, being darker.

The granules of the cytoplasm are colored by neutral anilin dyes. Acid dyes, like eosin, and the basic dyes do not affect them. With the Ehrlich-Biondi stain, the neutrophilic granules are tinted purple or violet. They are small and irregular in size and shape. A high power of the microscope is necessary to define them. In normal blood the neutrophilic granules are rarely found except in the polymorphonuclear cells. Occasionally the large lymphocytes contain a few, and sometimes they are present in the so-called *transitional leukocytes*. Neutrophilic leukocytes are found only in man. According to Stengel, the neutrophilic granules take both the acid and the neutral stains.

2. **The Lymphocyte.**—The essential differential feature of the lymphocyte is the absence of granules in the cytoplasm.

(*a*) *The small lymphocyte* is a little larger than the red blood corpuscle, and consists of a large round nucleus rich in chromatin, with a thin layer of cytoplasm surrounding it. The cytoplasm is often invisible and is entirely free from granules of any kind.

These cells comprise from 20 to 30 per cent. of the leukocytes, and have an average diameter of about 8 to 9 μ. Cabot believes that the small leukocyte is the youngest form of colorless blood corpuscle, and represents the cell exactly as derived from the lymphoid tissues. He points out, however, that the blood does not show all the intermediate steps between it and the forms thought to be older.

(*b*) *The Large Lymphocyte.*—There is no sharp line of distinction between this and the preceding cell. The chief difference is that it is larger than the small lymphocyte. There are, however, other minor differences. Thus, the nucleus of the small lymphocyte stains more deeply than that of the larger cell. The large lymphocyte also contains relatively more cytoplasm, which is continually without granules. The small lymphocyte is not ameboid and not phagocytic. The large lymphocyte, which is called by Hankin and Hardy the hyaline cell, and spoken of by Metschnikoff as a *macrophage*, is both ameboid and phagocytic, and may be one of the most important phagocytic cells of the body.

3. **The Transitional Leukocyte.**—Certain of the large lymphocytes, or perhaps more correctly certain lymphocytes, more closely resembling the large lymphocyte than any other form of leukocyte, present a peculiar indentation of the nucleus, and sometimes contain a few neutrophilic granules. These cells are spoken of as *transitional leukocytes*, and are looked upon as corpuscles in a transitional stage of development—intermediate between lymphocyte and polymorphonuclear. Cabot says—and rightly—that this lenkocyte has no more right to be called transitional than any other. If one is transitional, all are transitional.

4. **The Eosinophilic Leukocyte.**—Those who adhere to the transitional theory of leukocyte origin regard this corpuscle as the oldest form. It is thought to be about to disintegrate. Cabot describes them as leukocytes that are "overripe." This opinion is based upon the fact that the eosinophilic cells are less cohesive than the others. These cells are present in the normal blood in small numbers, forming not more than 3 per cent. according to the majority of observers. They are cells of moderate size, usually measuring about 12 μ in diameter; the nuclei are polymorphic in shape, and the cytoplasm is characterized by the presence of large numbers of coarse, spheric granules, with a marked affinity for acid anilin dyes, especially for eosin and acid fuchsin. They are also called oxyphilic granules by Ehrlich, and also *x*-granulations. In the Ehrlich-Biondi specimens the granules are of a copper or burnt-sienna color, some staining more deeply than others in the same cell. Occasionally they stain black with osmic acid, which has led some observers to believe that they are fatty in nature.

The granules appear evenly distributed throughout the cytoplasm, but seem to be free to move about in it, and in stained specimens of dry blood-films they never overlie the nucleus, but surround it, loosely scattered in the cytoplasm. This observation seems to have been first made by Cabot. In living blood the eosinophilic cells are ameboid. It is a question whether or not they are phagocytic, but most hematologists believe so. Some think that the oxyphilic granules they contain consist of highly germicidal substances by which the system copes with infectious bacteria. Occasionally, when living blood is observed under the microscope, granules are seen to escape from the cytoplasm and float away. According to Sangree, the escaped granules are motile. The eosinophilic cells are usually a little smaller than the neutrophiles, and are less regular in shape. The nucleus of the former is usually pale, and in Ehrlich-Biondi specimens assumes a robin's-egg color and homogeneous staining.

5. **Basophilic Leukocytes.**—These have been called by some "mastzellen," or musting or feeding cells. They are present in the blood only in rare instances. According to Cannon, they are never present in the blood in health, except in children. Coles never met with a true "mastzelle" in the blood in health or disease. Cabot states that they do not occur in normal blood. In leukemia they are said not to be uncommon. The basophilic cells stain well with

basic anilin dyes, such as methylene-blue and dahlia. The cells are thought, by a majority of students, to be derived from the connective tissues. They are large cells whose cytoplasm is densely packed with granules, the γ-granulations of Ehrlich, which are rather coarse and obscure the nucleus. It is thought by some that these cells cannot pass through the terminal capillaries.

6. **The Myelocyte.**—The myelocyte has no normal existence in the blood. It is a large cell, often six or seven times the diameter of an erythrocyte, but usually somewhat smaller, and, according to Cabot, has an average diameter of 50.75 μ. It is found in the blood in intoxication, in starvation, and in the primary anemias. In large numbers it characterizes the disease known as leukemia. The cell can be recognized only when properly stained. It is a regularly rounded or oval cell, of large size, containing a single—rarely two—oval, homogeneous, robin's-egg color nucleus, and a moderate amount of cytoplasm with large numbers of neutrophilic granules. It differs from the large lymphocyte essentially by the presence of its granules, and from the polymorphonuclear leukocyte by its single rounded nucleus and larger size. It exactly resembles cells which are normally found in the bone-marrow, and it is commonly believed that it enters the blood from the bone-marrow. Cabot, however, who adheres strongly to the transitional theory of leukocytic development, regards this corpuscle as an intermediate stage between the large lymphocyte and polymorphonuclear leukocyte.

The chief variations in number affect the polymorphonuclear and eosinophile leukocytes. The former of these is subject to variations depending upon conditions to which attention will be called when we come to consider leukocytosis. The variation in the number of eosinophiles is not so clearly understood.

Leukocytosis.—When the leukocytes are increased in number, the condition is usually described as leukocytosis. It would, however, be more nearly correct to speak of the condition as *hyperleukocytosis*. Cabot says it is "an increase in the number of leukocytes in the peripheral blood over the number normal in the individual case; this increase, never involving a diminution in the polymorphonuclear varieties, but generally a marked, absolute, and relative gain over the number previously present." Hyperleukocytosis may be of two varieties—the ordinary *leukocytosis*, in which the polymorphonuclear cells are increased in number, and *lymphocytosis*, in which the lymphocytes are increased in number; the latter condition is essentially pathologic. The opposite condition, in which the leukocytes are decreased in number, is described as *hypoleukocytosis* or *leukopenia*. Inasmuch as different authorities are not in accord concerning the number of leukocytes normally present in the blood, it is difficult to define exactly what number of corpuscles will constitute a hyperleukocytosis. Stengel advises that when the number of leukocytes shall exceed 10,000 per mm., it is to be so regarded. In moderate hyperleukocytosis 20,000 to 30,000 may be observed; in marked hyperleukocytosis 40,000 to 50,000 are observed. In distinctly pathologic conditions the number of leukocytes may increase to several millions. Hyperleukocytosis may be physiologic or pathologic.

(*a*) **Physiologic hyperleukocytosis** occurs under conditions that must be regarded as normal or on the border-line between the normal and the abnormal.

1. **Leukocytosis of the New-born.**—At birth an infant has in the neighborhood of 6,000,000 erythrocytes in the blood, and with this a number of leukocytes varying from 15,000 to 35,000 per c.mm. At six months the number is reduced, but the normal standard is not reached until the second, sometimes not until the sixth, year. Hayem found a new-born infant to have 18,000 leukocytes; at the end of the first month, 8000; from the first month to the fourth year, 6000; adults, 5000. Cabot finds the normal standard for the adult 7500 leukocytes. The new-born infant he finds to have from 17,000 to 36,000 leukocytes; at six months he gives 12,000 as the number, and asserts that the normal standard is not reached for several years. According to Rieder, the mononuclear leukocytes or lymphocytes predominate. Various theories have been offered to explain the condition—probably it depends upon the continuous and protracted digestive efforts of infancy. By some it is thought that it is caused by inspissation of the blood.

2. **Leukocytosis of Digestion.**—Total abstinence from food lowers the number of leukocytes in the blood. In the blood of professional fasters, among whom the Italian, Succi, has been studied, the number of leukocytes in the first week's fast descended to 861 per c.mm. After the first week it rose to 1530 and remained there throughout the rest of the thirty days' abstinence.

The hyperleukocytosis of digestion is not invariable, but occurs with such regularity and so modifies the actual condition of the blood that Stengel has suggested that blood counts be made as nearly as possible in the hours just preceding the midday meal, and every blood count be accompanied by accurate data as to the time of the last meal, the kind of food consumed, and any peculiarity in the quality of the food last taken by the patient.

The maximum hyperleukocytosis is reached in three or four hours after eating, and disappears within six or eight hours afterward. Proteid foods are most marked in their effect upon the number of corpuscles in the blood.

In cases where abstinence is asserted and malingering suspected, an examination of the blood will often make clear the nature of the case. After a meal rich in proteid foods, 10,000 leukocytes may perhaps be considered an average for a healthy person. Cabot found that when the number of leukocytes present in the blood before the meal was small, the subsequent increase in number does not exceed 7000 leukocytes. Any disease of the gastro-intestinal apparatus may modify or prevent the occurrence of the hypoleukocytosis of digestion. Thus, according to Müller, it is constantly absent in carcinoma of the stomach. In anemia and debilitated conditions no hyperleukocytosis follows the ingestion of food. The more unusual the food taken by the individual, the more marked the hyperleukocytosis that follows. In the hyperleukocytosis of digestion the relative proportion of the different leukocytes is not altered, with the possible exception that the eosinophilic cells are sometimes diminished in number.

3. **Hyperleukocytosis of Pregnancy.**—This occurs, as a rule, in the later months of pregnancy, and is not invariably present. It is of no use as a diagnostic sign of the condition because of the irregularity of its occurrence. The cells increase to about 13,000, and with the beginning of labor may ascend to 15,000 or 18,000. The cause of this form of hyperleukocytosis is unknown.

4. **Hyperleukocytosis of the Postpartum State.**—It is important to remember that such a condition takes place, lest it be mistaken for a sign of septic infection or concealed hemorrhage. Cabot gives 15,000 cells as an average count during the first week. Sometimes, however, the cells ascend to 35,000.

5. **Hyperleukocytosis Resulting from Exercise, Massage, and Baths.**—All these conditions increase the number of leukocytes in the blood. Thayer counted the leukocytes of his own blood and found them markedly increased after a cold bath. Counting the leukocytes of a typhoid patient immediately after a Brand bath, he found that they had ascended from 7724 to 13,170. The leukocytosis resulting from exercise is given by Cabot at from 11,000 to 13,000 cells.

6. **Agonal Hyperleukocytosis.**—This is leukocytosis of the moribund condition. It is not present in all cases, but is more common where death takes place slowly. Cabot found it very marked in cases of pernicious anemia, where the corpuscles counted on the day of the patient's death were one white for every fifteen red. The chief increase is in the polymorphonuclear cells. Stengel thinks this form of hyperleukocytosis depends upon the reduction of blood-pressure by which the discharge of leukocytes from the lymphatic organs into the circulation is permitted. Flexner's investigations upon the terminal infections must not be forgotten in this connection, and many of the agonal hyperleukocytoses depend upon terminal infection.

(*b*) **Pathologic hyperleukocytosis** takes place under purely abnormal conditions.

1. **Posthemorrhagic Hyperleukocytosis.**—Within a short time after the occurrence of a considerable hemorrhage the number of corpuscles in the blood is subject to a marked increase—15,000 cells is not unusual; 16,000 to 18,000 cells have been noted.

It is said that in gastric hemorrhage this hyperleukocytosis disappears within a day or two, but in ordinary traumatic hemorrhage it may persist longer. According to Stengel, the lymphocytes may be strikingly increased.

2. **Hyperleukocytosis of Infection.**—The extent of the hyperleukocytosis seen in infection and inflammation will depend upon the extent and severity of the lesion. Croupous pneumonia shows the most marked increase in the number of cells, which increase to from 45,000 to 114,000 per c.mm. In suppurative lesions there is marked increase, and in cases of suppurative appendicitis Stengel has counted from 15,000 to 40,000 cells. No direct connection seems to exist between hyperleukocytosis and fever. Acute, rapidly spreading inflammatory conditions, except in cases of abscess, well isolated by encapsulating walls, usually show the most marked increase in the number of leukocytes. It is said the inflammatory hyperleukocytosis is preceded by a temporary hypoleukocytosis. Moderate hyperleukocytosis has been found in acute rheumatism, diphtheria, variola, scarlatina, anthrax, and occasionally in measles. In small-pox the hyperleukocytosis is usually in direct proportion to the severity of the eruption.

3. **Hyperleukocytosis of Intoxication.**—This form of hyperleukocytosis occurs in poisoning by illuminating-gas, quinin, during etherization, and in such diseases as gout and acute yellow atrophy of the liver. It is difficult to differentiate from the therapeutic and infectious hyperleukocytosis.

4. **Hyperleukocytosis of Malignant Disease.**—If we regard sarcoma and carcinoma as infectious diseases, the hyperleukocytosis accompanying them must properly be classified as infectious. In the absence of any proof of the infectious nature of the disease, however, it is well to make a separate group for them. The most marked hyperleukocytosis occurs in sarcoma, in which the number of white corpuscles may increase to 50,000 or more. The lymphocytes and other mononuclear elements are conspicuous, and often the eosinophiles are greatly increased. The cause of the leukocytosis is unknown; some think it dependent upon the absorption of poisonous products from the tumor.

5. **Hyperleukocytosis of Marasmus.**—The hyperleukocytosis accompanying the cachexia of carcinoma has been mentioned in the preceding paragraph. Other conditions, however, such as congenital syphilis and rachitis, are also sometimes accompanied by pronounced increase in the number of leukocytes in the blood—indeed, sometimes so pronounced as to suggest leukemia. Some of these conditions are akin to the infectious diseases, but the leukocytosis differs from that of infection.

6. **Experimental and Therapeutic Hyperleukocytosis.**—When injected hypodermically or administered by the mouth, pilocarpin, oil of turpentine, oil of cinnamon, oil of peppermint, tuberculin, camphor, urea, extracts of the spleen, thymus gland, and bone-marrow cause marked hyperleukocytosis. Tonics and stomachics, especially tincture of gentian, have a slight effect in increasing the leukocytes. Camphor has also a pronounced effect. Intravenous and subcutaneous injections of hemialbumose, peptone, pepsin, nucleinic acid, nuclein, pyocyanin, curare, and uric acid also are followed by increase in the number of leukocytes. Goldschneider and Jacob found that the extract of pancreas, thyroid, kidney, and liver would not produce increase in the number of leukocytes.

Bacterial poisons, when given in fatal doses, reduce the number of leukocytes. When the dose is insufficient to cause the death of the animal, there is a primary reduction, followed by increase in the number of leukocytes. When animals have been immunized to bacterial poison, an injection of it produces no change in the number of leukocytes in the blood.

7. **Leukemia.**—In this disease the most marked hyperleukocytosis takes place. The leukocytes may be one to ten, one to five, or one to one, and, according to Osler, may *even in exceptional cases outnumber the red corpuscles.*

The origin of the leukocytes in hyperleukocytosis is by no means clear. Virchow was of the opinion that the leukocytes increased in number because of stimulation of the blood-making organs, that the leukocytes transformed themselves into erythrocytes, and that in hyperleukocytosis there was a retarded transformation of the white corpuscles into the red. Löwit and others are of the opinion that the increased number of leukocytes depends upon the regenerative effort following destruction of preëxistent leukocytes. These observers find hyperleukocytosis to be preceded by hypoleukocytosis. This is not, however, always the case. Many observers, among whom is Buchner, think that micro-organismal products and metabolic products with chemotactic effects are the cause of hyperleukocytosis, so that the increase in the number of leukocytes in the circulating blood is the result of an attractive influence exerted upon the free leukocytes within the blood-making organs. Ehrlich has observed the bone-marrow to be unusually active, converting mononuclear cells of the marrow into polymorphonuclear leukocytes. Schultz originated the theory of disturbed distribution, having been led to conclude that the increased number of leukocytes in the peripheral circulation occurred simultaneously with a corresponding diminution in the central circulation. Von Limbeck looks upon leukocytosis as of chemotactic origin, and points to the close relationship existing between hyperleukocytosis and inflammatory exudation. Probably the most widely accepted theory of the present time is that of Goldschneider and Jacob, who followed the footsteps of Buchner and others, and found that injections of bacterial products resulted in a preliminary hypoleukocytosis followed by hyperleukocytosis. The more powerful the influence upon the leukocytes, the more marked the hyperleukocytosis. The operation is twofold, the leukocytes at first being repelled and collecting in the capillaries, particularly in the lung, and, secondly, an attractive force exerted upon the blood-making organs and leading to an increased output of leukocytes already formed or perhaps also a new formation of leukocytes.

Schultz was probably correct about the disturbance of distribution of the leukocytes, as the leukocytes which disappear from the peripheral circulation collect in the capillaries of the lung, etc. There is no reason to believe that the increase in the number of leukocytes depends upon any marked efforts at leukocytic karyokinesis. While it is true that Fleming and others have occasionally found mitotic leukocytes in the circulating blood, their occurrence there is very unusual.

Hypoleukocytosis or **leukopenia** indicates a diminution in the number of white blood corpuscles in the peripheral circulation as compared with the number normal for the given individual. We meet with the same difficulty when considering hypoleukocytosis that confronted us in connection with hyperleukocytosis—that is, the establishment of a standard by which to judge the variation from the normal. Stengel suggests that all cases in which the leukocytes are below 6000 in number be regarded as hypoleukocytosis. The cause of hypoleukocytosis is usually thought to be what Löwit describes as *leukolysis*, or destruction of leukocytes. The condition is seen in starvation, baths which, because of their high temperature or prolonged duration, become exhausting, in pernicious anemia, and in certain of the infectious diseases. The hypoleukocytosis of the infectious diseases is very important for consideration, because the rule is that infection shall be accompanied by hyperleukocytosis. Hypoleukocytosis is, however, the rule in influenza, measles, miliary tuberculosis, malaria, and typhoid fever, in the later weeks of which it is invariable and accompanied by lymphocytosis. In rare cases croupous pneumonia exhibits hypoleukocytosis instead of the usual hyperleukocytosis. Under such circumstances the prognosis is usually bad. Stockton has reported a case of a child suffering from croupous pneumonia with relapse in which there was hypoleukocytosis. The case recovered.

Lymphocytosis.—Upon several occasions it has been necessary to state that the lymphocytes were increased in conditions of hyperleukocytosis, and to distinguish between lymphocytosis and leukocytosis, the former of which conditions has to do with the polymorphonuclear cells, the latter with the lymphocytes. Lymphocytosis occurs in the following conditions:

In infancy as a normal condition; in marasmatic affections, such as rickets, hereditary syphilis, and scurvy; in the anemias, especially chlorosis, pernicious anemia, the anemia of syphilis, the later weeks of typhoid fever, and in lactation; in hemophilia; in strumous affections, such as goiter, exophthalmic goiter, cervical adenitis; after taking thyroid extract, and in certain tumors, especially of the spleen, and in certain irregular cases, especially those associated with ague-cake; at the end of scarlatina, pneumonia with delayed resolution, measles, phthisis, and the non-suppurative cases of smallpox.

Eosinophilia, or increase in the percentage of eosinophilic corpuscles in the circulating blood, may occur with or without an increase in the total number of leukocytes. Leukemia is usually associated with some increase in the eosinophilic cells—according to Cabot, from 1 to 3 per cent. Infants have a larger proportion of eosinophilic cells than adults.

Sarcoma, leukemia, osteomalacia, pemphigus, pellagra, diseases of the ovaries, prostatitis, gonorrhea, ovarian tumor, puerperal mania, disturbances of the sympathetic system, and exophthalmic goiter are said by various authorities to be accompanied by increase in the number of eosinophilic cells.

Parasitic diseases, such as ankylostomiasis and trichiniasis, are accompanied by increase in the number of eosinophilic cells. In 3 cases of trichiniasis studied by Thayer there was an enormous increase in the number of eosinophilic cells—45.2 per cent. Brown observed 2 cases of trichiniasis in which, with 4,200,000 erythrocytes, there was 37 per cent. of eosinophilic cells, which gradually declined 10 to 15 per cent. and then gradually ascended for three weeks, reached 68.2 per cent., the highest percentage of eosinophilic cells ever recorded ; two-thirds of all the leukocytes were of the eosinophilic variety. The three important features of these cases are the marked increase in the number of eosinophilic cells, the coincident fall of the neutrophilic cells, and the marked leukocytosis. In malaria with high fever the number of eosinophilic cells is apt to be increased.

Eosinophilia is always present in gout, bronchial asthma, uremia, oxaluria, epilepsy, etc. According to Cabot, the eosinophilic cells diminish in number during digestion, after castration, in the febrile stages of influenza, pneumonia, typhoid, diphtheria, and most of the infectious diseases accompanied by hyperleukocytosis. Malignant disease and hemorrhage also diminish the number of eosinophilic cells.

Myelocytosis.—Myelocytes are always of pathologic significance. Small numbers of them may occur in the blood in uremia, CO_2-poisoning, diabetes, syphilis, sarcoma, and in a variety of other infections. They are of almost invariable occurrence in all the grave forms of anemia, and occur in large numbers in leukemia and in moderate numbers in pernicious anemia. In one disease, leukemia, they may form the bulk of the leukocytic element of the blood, and be present in such numbers as entirely to outweigh other forms.

Hyperinosis.—This term is used to signify an increase of fibrin factors in the blood. As is well known, fibrin does not exist as such in the circulating blood, but under various pathologic conditions is formed by the union of fibrin ferments, probably derived from the leukocytes and fibrin factors, of which fibrinogen and fibrinoplastin are the most important. Hyperinosis, therefore, really signifies increase in the amount of fibrin factors in the blood. The presence or absence of calcium salts may also be of importance in this connection. Schmidt, having shown that for the formation of fibrin the union of fibrinogen and a ferment, of which he describes *prothrombin* and *zymoplastin* as derived from destroyed leukocytes, is insufficient to bring about the formation of fibrin except when calcium salts are present. Cabot says the amount of fibrin formed in the blood can be taken more or less as an index of the condition in which the patient found himself when the blood was secured. Both the quantity of fibrin formed and the rapidity of its formation are facts of importance for observation and study.

As a rule, one can say that the fibrin factors are increased in those conditions in which the leukocytes are increased in number. This would seem to indicate that were the fibrin factors not increased, the fibrin ferment, if derived from the leukocytes, might be capable of producing an unusual amount of fibrin with unusual rapidity. The toxic products of certain bacteria also have a strong potency as fibrin ferments ; especially is this true of the products of diphtheria and pneumonia. Whether, however, the increased amount of fibrin in the blood in the latter affection has anything to do with the micro-organism is difficult to prove, because of the marked hyperleukocytosis which characterizes the disease. Fibrin is generally increased in the infectious diseases, and especially in the inflammatory diseases. The most marked increase is seen in pneumonia, acute articular rheumatism, suppuration, and in scorbutus. In miliary tuberculosis and the early stages of influenza it is diminished. Fibrin is also diminished in those conditions in which the blood shows hydremia. Especially is this true of pernicious anemia.

In the symptomatic anemias and in leukemia the amount of fibrin is not altered. Cabot points out that the absence of hyperinosis in malignant disease is of importance as a differential point between it and suppurative affections. The formation of fibrin is delayed to an unusual period in hemophilia. Indeed, in some cases of this disease it would seem as if no fibrin was formed.

The Blood Plaques.—These appear as circular discs somewhat resembling erythrocytes, but much smaller. They are colorless and devoid of the characteristic double concavity. The size is somewhat variable—rarely above $3\ \mu$ in diameter, often much less. They are peculiarly viscid in nature, and in drawn blood unite in clusters or agglutinations, which are prone to adhere to the erythrocytes or leukocytes. Their number has been variously estimated by different observers at from 150,000 to 250,000 per c.mm. A few authorities have even counted as many as 500,000 per c.mm. Many theories as to their origin and function have been suggested, some, as Löwit, regarding them as artefacts, others, as Hayem, looking upon them as hematoblasts or red blood-corpuscle formers. They stain readily with anilin dyes, giving an amphophilic reaction. Methylene-blue colors them quite well. They seem to play no important rôle in pathologic conditions, but are somewhat reduced in number in febrile affections. It is also said that they are of importance in connection with the formation of thrombi.

Lipemia.—Many have observed small free granules, spheric in shape and colorless, floating among the corpuscles. They have been variously looked upon as micro-organisms, granules escaped from leukocytes, animal parasites, and foreign matter. The granules very frequently stain with osmic acid, and, therefore, are strongly suggestive of fat. Von Jaksch asserts that the blood always contains small quantities of fat, especially during digestion. Grawitz found fat rising to the surface of blood contained in capillary tubes, like cream upon milk. It is possible for globules of fat to enter the drop of drawn blood from the skin, but the amount found is at times sufficient to make certain that it preëxisted in the circulating blood. According to Cabot, fatty globules are of frequent occurrence in phthisis, diabetes mellitus, obesity, alcoholism, nephritis, and occasionally in health. Considerable quantities of fat, sufficient to occasion embolism, occasionally gain entrance to the blood in the case of fracture of the shaft of long bones.

Melanemia.—The presence of pigment in the blood takes place most commonly in chronic malaria. It is chiefly to be seen during or shortly after a paroxysm. Free pigment is found only at the time at which the segmentation of the parasites takes place. Usually the pigment is found in the bodies of the leukocytes, and from them is transferred to the capillaries and tissue-cells. Occasionally pigment occurs in the blood in relapsing fever, and sometimes in Addison's disease—in the latter chiefly in the form of yellowish-brown or brownish-black granules, sometimes as bacillary fragments.

THE PRIMARY ANEMIAS.

Pernicious Anemia.—Pernicious anemia is a disease of hematogenesis characterized by the appearance of large numbers of imperfectly formed red corpuscles in a generally impoverished blood. This disease was first described by Addison as—"A general anemia occurring without any discoverable cause whatever, in cases in which there has been no previous loss of blood, no exhausting diarrhea, no chlorosis, no purpura, no renal, splenic, miasmatic, glandular, strumous, or malignant disease." It occurs in nearly all parts of the world, and is most common after middle life, though it occurs at all ages, even in childhood. It is probably more common in women than in men. It depends upon some as yet unknown cause, probably, however, some form of intoxication. Insufficient and improper food; nervous disturbances, such as violent shock; pregnancy and lactation; gastro-intestinal diseases, such as atrophy of the stomach and interstitial gastritis; parasitic diseases, such as ankylostomiasis and bothriocephaliasis; frequently repeated hemorrhages; general diseases, infectious diseases, and intoxications have been supposed to predispose to its development.

Morbid Anatomy.—The body of the patient is rarely emaciated; indeed, he may be unusually stout. In most cases the skin, conjunctiva, and other mucous membranes show a peculiar lemon tint. There is usually some dropsy about the ankles; there may be extreme anasarca. Upon opening the body the muscles are found to be intensely red in color, resembling horse-flesh, and contrasting markedly with the pale-yellow fat. Sometimes the fat is lemon-colored. Hemorrhages are common on the skin and upon the serous surfaces; there may be effusions into the serous cavities.

The heart is large, flabby, and empty, its muscular substance often intensely fatty and of a pale-lemon color. Osler says: "In no condition do we see more extreme fatty degeneration." The muscular substance is not uniformly affected, but the degenerated areas are distributed in such a manner as to give the organ a mottled appearance, often described as "tabby-mottling." The fatty degeneration may also affect the diaphragm and peripheral muscles. The lungs show no special changes. The stomach may be normal or may be atrophic. The mucosa may be extremely atrophied, with fatty degeneration of its tubules. The overgrowth of connective tissue in the walls of the stomach may reduce its size almost to that of an infant, and throw the mucous membrane into folds or rugæ. The liver may be enlarged and fatty. It has been found to contain an unusual quantity of iron, which can readily be demonstrated in microscopic sections, treated with chemically pure ferrocyanid of potassium and hydrochloric acid. The iron appears blue, and is situated in the outer and middle zones of the lobules, sometimes seeming to follow the course of the bile-capillaries. The spleen shows no important changes: it may be very small and sometimes contains iron in excess. The kidneys are enlarged, their color pale, the contrast between cortical and medullary substance faint. High-grade degeneration of the tubules with fatty metamorphosis of the cells, most pronounced in the convoluted tubules, is usually present. The glomeruli show no particular alterations. The lymphatic glands may be of a deep-red color. A considerable amount of iron is to be found in the convoluted tubules of the kidney. The adrenal bodies are not altered. The bone-marrow may resemble that of a child, changing from the normal fatty to the fetal or lymphoid condition. This change may occur in local punctiform areas or be uniformly distributed. It is characteristic in the long bones only, and is best studied in the shaft of the tibia. Microscopically, a vast increase is observed in the nucleated erythrocytes in the marrow, with a concomitant atrophy and sometimes an entire disappearance of fat-cells. These changes are not peculiar to pernicious anemia. Interesting changes have also been discovered in the

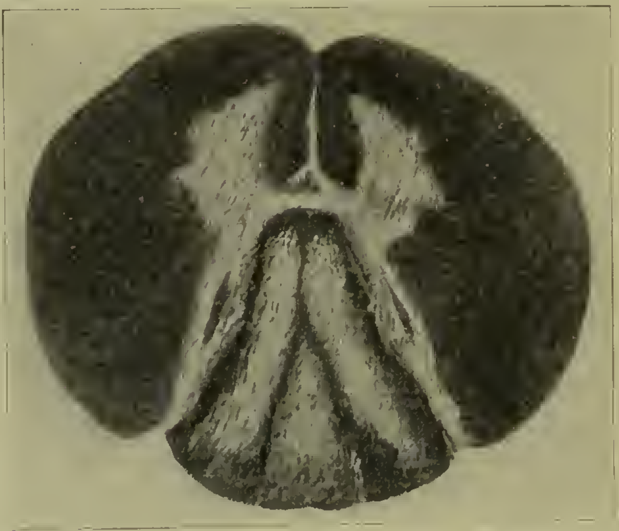

FIG. 228.—Section of spinal cord, cervical swelling, from a case of pernicious anemia (Burr).

central nervous system in the form of degeneration of the posterior columns of the cord in pernicious anemia. The lesions are symmetric and resemble those of other intoxications.

The blood changes are of chief interest. It may be difficult to secure a drop of blood, as the patients do not always bleed freely. As the blood escapes from the puncture, it sometimes appears pale and watery and sometimes streaked; its fluidity seems to be increased, and its coagulation deferred. Rouleau formation may not occur. The erythrocytes vary greatly from the normal in shape and size, and in the presence of large numbers of nucleated cells. Microcytes, macrocytes, megalocytes, and poikilocytes are all very common.

Hayem found one-eighth of all the erythrocytes to be megalocytes. The microcytes may be spheric in shape. There is no particular form of the poikilocytes characteristic of pernicious anemia. The cells may be stellate, clavate, fusiform, etc. Litton thinks horseshoe-shaped cells most frequent in pernicious anemia. Cabot has seen a case in which the erythrocytes were all club-shaped, looking like a lot of gigantic bacilli. Their shapes frequently vary as well as their size. In stained specimens there may be vacuoles, and whitish spots or streaks in the substance of the corpuscles. Occasionally one sees a corpuscle whose center seems to be perforated. Polychromatophilic erythrocytes are common, and nucleated erythrocytes which stain in this manner are sometimes difficult to distinguish from lymphocytes. Normoblasts and megaloblasts may be many or few and difficult to find. Megaloblasts are said to be of bad prognostic significance.

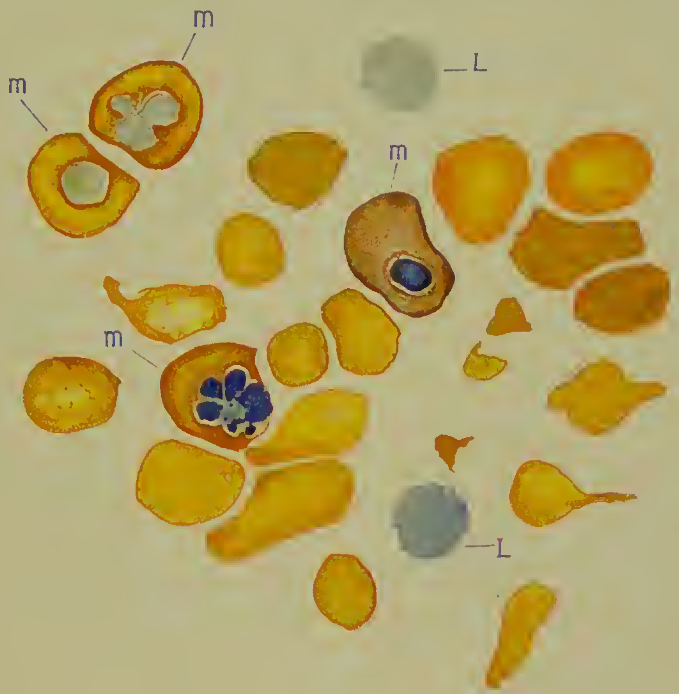

FIG. 229.—Pernicious anemia: L, L, Lymphocytes; m, m, m, m, megaloblasts; cover-slips stained with Ehrlich's triacid, and drawn with camera lucida (Cabot).

Shadow cells are sometimes present, though rarely in large numbers. Blood crises are said to occur, and to cause the paroxysmal and unexpected appearance of a large number of normoblasts, remaining in the blood from four to six days. Such blood crises are said to be followed by a great increase in the number of blood corpuscles. The blood plaques are diminished in number, and the fibrin is diminished in quantity. A great variation in the size and shape of the corpuscles, of which the number is markedly reduced, is always present. In 10 cases studied by Stengel there was an average of 1,134,000 erythrocytes. An average of Cabot's 52 cases showed 1,200,000. There may be very few corpuscles, a case having been reported by Quincke in which there were only 143,000.

The hemoglobin is always considerably reduced, but while thus absolutely reduced, is relatively increased, so that with 1,000,000 erythrocytes 30 to 35 per cent. of hemoglobin is the usual ratio.

The leukocytes seem to play no conspicuous or important part in the blood changes. In the earlier stages they may be decreased in number, but there may be a normal number or they may be increased. Cabot finds a marked leukopenia, as a rule. Of the leukocytes, the small lymphocyte is the most numerous. In 34 cases which Cabot studied the lymphocytes numbered 34.9 per cent. of all the leukocytes. Stengel found that toward the end of the disease the leukocytes increase in number, sometimes giving rise to a suspicion of leukemia. The terminal or preagonal leukocytosis sometimes becomes excessive. Eosinophile cells are occasionally increased. In 49 cases which Cabot examined, the average was 2.7 per cent. In one case, however, he observed 6.6 per cent. and in another 9 per cent. Occasional myelocytes occur. According to Cabot, the myelocyte is more common in pernicious anemia, and is present in greater number than in any other disease except leukemia. The specific gravity of the blood is usually diminished; this would be expected from its markedly hydremic character. Quincke found it 1.0282; Stengel, 1.025 in one case. The amount of albumin present is less strikingly reduced than might be expected from the diminution of the blood.

Chlorosis.—This is a primary or essential anemia, usually affecting girls during the period of adolescence, and characterized essentially by a reduction in the amount of hemoglobin, with or without diminution in the number of the corpuscles. Cases in which the corpuscles are not diminished in number have been called *pseudochlorosis*, while *chlorosis* is reserved for cases in which the hemoglobin and corpuscles are both diminished. The disease is commonly known among the laity as the "green sickness." It affects both men and women, though women suffer much oftener from it than men. It is most common between the fourteenth and seventeenth years. Blondes are probably more frequently affected than brunets. The disease sometimes occurs in early childhood, but is very rare at that period. The cause of the disease is unknown.

It has been thought by many to have some connection with the development of the sexual function. Virchow pointed out that in many cases there was a defective development of the circulatory system; perhaps Rokitansky was the first to show that the heart was sometimes abnormally small, and that in some cases there is hypoplasia of the aorta and great vessels. The vessels are usually very elastic; the heart is often dilated, and the left ventricle hypertrophied. There may be degeneration of the heart. It is said that there is sometimes a tendency to endocarditis, also to venous thrombosis. In some cases defective development of the sexual organs has been observed. Rarely a family predisposition to the disease can be made out. Bad hygiene, improper diet, overwork, nervous and emotional disturbances, homesickness, disturbances of the menstrual function, seem at times to play some part in the etiology of the disease.

Sir Andrew Clark was of the opinion that chlorosis was the result of constipation, with absorption of poisonous substances from the intestine into the blood. He describes it as **copremia**, the result of coprostasis. Meinert believed the disease to depend upon displacement of the abdominal organs from tight dressing at the waist, with irritation of the splanchnic nerves and consequent disturbances of innervation in the spleen and other blood-making organs. According to this view, chlorosis results from gastro-enteroptosis. Occasionally there is a family history of tuberculosis, and sometimes hysteria has appeared to have an influence in the production of the disease. The patients present an extreme greenish pallor of the skin and are thin and emaciated, though they are often stout and well nourished. The pallor of the skin and the blanched conjunctiva and other mucous membranes constitute the visible characteristics of the disease. The blood is chiefly affected. It is characterized by the presence of small, pale, sometimes deformed erythrocytes, whose number, as we have already pointed out, may or may not be decreased, according to the severity of the case.

The hemoglobin is always markedly reduced in quantity. Hyperleukocytosis is rarely present except in cases accompanied by infection or other accidental causes. The amount of fibrin in the blood is increased. In almost all cases some normoblasts are present. As the blood flows from the finger, it may be very pale. In 16 cases of chlorosis studied by Stengel the lowest blood count was 1,500,000 erythrocytes. In the lowest of 40 cases studied by Thayer there were 1,932,000 corpuscles, while the average number for each patient was 4,225,181. The percentage of hemoglobin in Thayer's cases was 44.1. Hayem has seen the erythrocytes as low as 1,662,000, and in one case, 937,360. Cabot studied 77 cases, in which the lowest blood count was 1,933,000 erythrocytes, the average number being 4,050,000. Occasionally the erythrocytes may be present in unusually large numbers. Thus, in one of Cabot's cases there were 7,100,000 erythrocytes. The number of erythrocytes in European statistics is considerably lower than in American statistics. The average amount of hemoglobin in Cabot's 77 cases was 41 per cent. The individual erythrocytes, when examined microscopically, often present characteristics easily recognizable to the experienced eye. Thus, they are usually paler than normal, especially at the center. In many cases the center of the corpuscle is invisible, the average diameter of the cell being somewhat diminished. Poikilocytosis is present in advanced and severe cases, causing them somewhat to resemble pernicious anemia, although the poikilocytosis of chlorosis probably never becomes so marked as in the other affection. Hayem never saw nucleated erythrocytes. Those seen are, for the most part, normoblasts, megaloblasts being very rare. Neudorfer has seen blood crises similar to those of pernicious anemia in which there was an unexpected appearance of large numbers of nucleated erythrocytes, followed by subsequent increase in the number of erythrocytes.

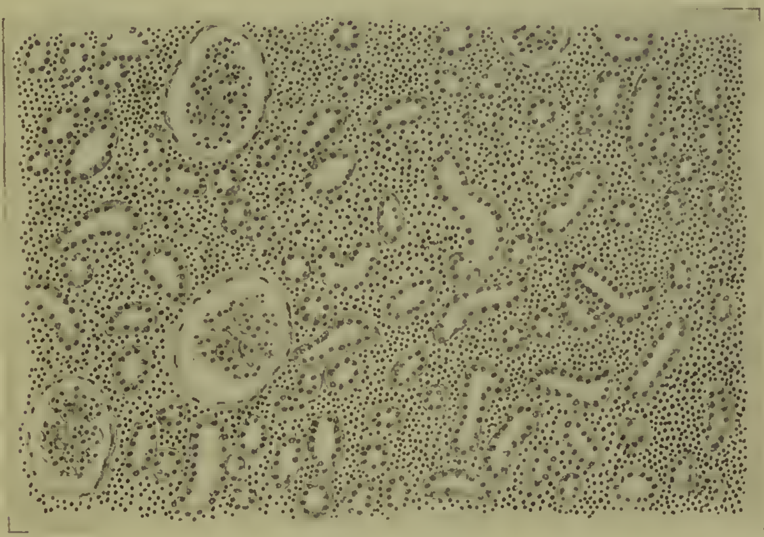

FIG. 230.—Kidney in acute leukemia. Urinary tubules and glomeruli crowded apart by dense uniform interstitial infiltration with lymphocytes (× 80) (Dürck).

The percentage of hemoglobin may be anywhere from 40 per cent. up. The specific gravity is reduced and may be as low as 1.030.

In 26 cases studied by Cabot the average number of leukocytes was 7485. In 63 cases studied by Thayer the average was 8467. The absence of hyperleukocytosis is the chief distinguishing point between chlorosis and the secondary or symptomatic anemias. The blood plaques are usually increased: Hayem found them always increased.

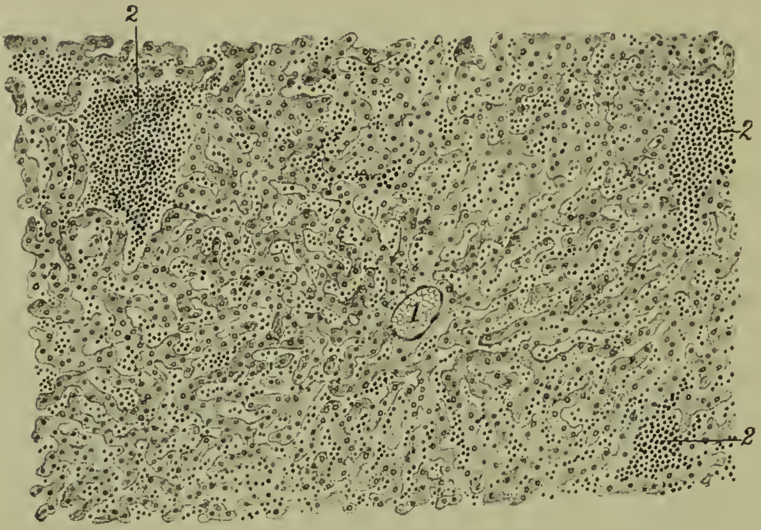

FIG. 231.—The liver in leukemia (leukemic infiltration): 1, Vena centralis, numerous lymphocytes in the portal capillaries between the columns of liver-cells; 2, 2, 2, periportal connective tissue infiltrated with radiating groups of lymphocytes (× 80) (Dürck).

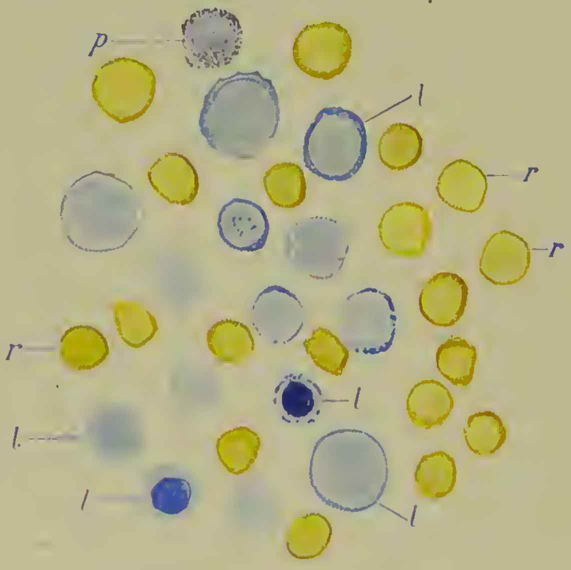

FIG. 232.—Lymphatic leukemia: *l, l, l, l, l*, Lymphocytes; *p*, polynuclear neutrophile; *r, r, r*, red cells (Cabot).

In chlorosis there is an occasional tendency to spontaneous thrombosis of the veins, most commonly occurring in the femoral vein, sometimes in the longitudinal sinus. The condition is seldom serious, though Truckwell has seen a case in which the thumb was lost from venous thrombosis.

Leukemia.—Leukemia is a disease of hematogenesis, characterized by an increase in the number of leukocytes in the circulating blood, and by characteristic changes in the bone-marrow, lymphatic glands, or spleen, or in all these structures, tending to run a more or less chronic course and marked by secondary lymphoid infiltration of various organs. It is usually a fatal affection, sometimes terminating in a few days, but more often continuing for several years. Intercurrent affections are common, and sometimes favorably influence the disease, though they are more frequently fatal. The disease was first mentioned by Bennet, of Edinburgh, in 1845, and called "suppuration of the blood." Its true nature was discovered by Virchow a few weeks later. It is customary to divide the cases of leukemia into three groups—the *splenic*, the *lymphatic*, and the *myelogenic*, according to the origin. Nothing is known of the etiology of the affection, but Löwit claims to have discovered an animal parasite which he thinks is the cause. The disease occurs in all parts of the world, but is uncommon in America. It occurs at all ages. Sanger saw it once in a still-born infant; Golitzinsky, a case in an infant one week old; and Osler has seen it in a babe eight months old. A number of cases in children from eight to ten weeks old are on record. It may also occur in old age. Men most frequently suffer from it in the third decade, women in the fourth decade. It is perhaps more common in men than in women, in the ratio of 67 to 32 per cent. Occasionally there seems to be a hereditary predisposition about the affection: thus, one case studied by Osler had three normal children one after the other, while one child born before the disease developed in the mother was leukemic. Cameron had a case whose grandmother, mother, and one brother were leukemic; and who had borne two children who died of the disease; she also had three healthy children. The lower animals as well as man are subject to leukemia. Malaria, syphilis, and traumatism have been put down as causes, but probably have nothing to do with the origin of the disease.

Morbid Anatomy.—There are two essential tissue lesions of leukemia. First, infiltration with leukocytes; second, hyperplasia of the lymphadenoid tissues. The body of the patient may be wasted; dropsy may be present. The heart may be distended and may contain greenish clots. When it is opened, the escaping liquid may be so rich in leukocytes as to be mistaken for pus; hence Bennett's mistake in regarding the disease as a "suppuration of the blood." Distention of peripheral veins is common. In the majority of cases the spleen is much enlarged, cases being on record in which it has weighed as much as twenty pounds. The condition is one of chronic hyperplasia, the capsule of the organ being thickened, its substance firm. It has a uniformly reddish-brown color; the Malpighian bodies may be invisible. Grayish-white, circumscribed, lymphoid masses may be distributed throughout the organ, contrasting strongly with the reddish-brown matrix, and bringing about a peculiar spotted, granite-like, or marbled appearance. In the early stages of the disease the pulp may be soft and the spleen extremely hyperemic. Rupture has sometimes occurred in such cases, and local inflammations caused by distention of the capsule are a common cause of adhesion between the spleen and neighboring organs. Hyperemic parts of the splenic substance contrast markedly with paler areas; sometimes areas of fatty degeneration are seen, probably resulting from pressure. Enlargement of the lymphatic nodes may occur concomitantly with the splenic enlargement, and may occur independently of changes in the spleen itself. The enlargement depends upon hyperplasia of the lymphoid elements; necrosis and fatty degeneration have been observed.

Occasionally incised lymphatic glands present a yellow-green appearance, such as is seen in chloroma. The changes usually affect chains of glands, the cervical being most frequently affected. There are almost always marked changes in the bone-marrow, which instead of being fatty in the shafts of the long bones, becomes dark in color, and not infrequently marked with small hemorrhagic foci resembling infarctions. Neuman described two forms which he calls pyoid and lymphoid bone-marrow. In the pyoid marrow there is a marked hyperplasia of the colorless marrow-cells; the marrow consists to a large extent of large, round, hemoglobin-free cells, with large pale nuclei and abundant fine neutrophilic granules. The lymphoid marrow contains many nucleated red blood corpuscles in all stages of development. Numerous cells with eosinophilic granules may also be found. The most common cell in the marrow is the myelocyte already described, which may become the most common cell in the blood. The thymus gland is usually enlarged. In a few cases the solitary glands of the intestine and the agminated glands of Peyer have been involved. Indeed, in a few cases Peyer's glands have been found ulcerated, their condition much resembling that of typhoid fever. The liver may be so enlarged as to weigh from 15 to 20 pounds, the increase depending upon diffuse leukemic infiltration, in which the columns of liver-cells are widely separated by leukocytes, partly within and partly without the capillaries. The chief infiltration occurs in the periportal area, the small vessels being densely packed with leukocytes. In the substance of the organ distinct lymphadenoid growths are occasionally found. Upon section the organ is variegated in appearance, with pale streaks or lines of lymphoid tissue in the darker liver substance.

The kidneys are often enlarged and pale, the capillaries distended with leukocytes. There may be leukemic infiltration throughout the whole organ, with accompanying atrophy and parenchymatous degeneration of the substance.

The adrenal bodies may be quite large. Lymphoid growths sometimes occur on the surface of the stomach and in the gastrosplenic omentum. The lungs rarely show any changes. While the leukemic infiltration and the lymphatic nodule formation are not infrequently encountered, Osler found distinct leukemic tumors but once in a series of 12 autopsies. In 159 cases collected by Gowers, there were only 13 instances of leukemic nodules in the liver and 10 in the kidneys. Such new growths may be composed of leukocytes that have left the capillaries. Bizzozzero has shown that in these tumors the cells are in process of active fission. There is sometimes a peculiar exanthematous eruption of the skin in leukemia, and beneath the skin one may find lymphoid infiltrations and nodules which soften, ulcerate, and lead to the formation of ulcers similar to those seen in mycosis fungoides.

The characteristic feature of the disease is a striking increase in the number of leukocytes, which may actually outnumber the erythrocytes. The leukocytes vary according to the form of the disease. Robin has seen a case in which there were twice as many white as red cells. In Cabot's large series, the average number of leukocytes is 438,000 per c.mm. The highest number he saw was 1,072,223. The appearance of the blood differs from that of hyperleukocytosis in that the increase in the leukocytes affects the *lymphocytes* or consists in the addition to the blood of immense numbers of *myelocytes*, while in hyperleukocytosis the increase is in the polymorphonuclear neutrophiles. Consisting of lymphocytes and myelocytes, the leukocytes of leukemia are not ameboid. Fleming, Hale, Spronck, and others have seen leukocytes undergo mitosis in the blood. Fatty degeneration of the leukocytes has been observed occasionally. When typhoid and miliary tuberculosis take place as intercurrent affections in individuals suffering from leukemia, the number of leukocytes becomes reduced, so that the blood condition temporarily improves. The number of leukocytes in any given case is subject to fluctuation, sometimes being double the number found at other times. This fluctuation takes place without any assignable cause. Stengel has seen the number of leukocytes fall from 150,000 to 30,000 under the influence of treatment.

In 10 cases studied by Cabot, the myelocytes numbered 37.7 per cent.; the eosinophiles, 4.4 per cent. Myelocytes may form 60 per cent. of all the leukocytes. The leukocytic alterations in the splenic and myelogenic forms of leukemia are too characteristic to allow any other disease to be confounded with it. Cabot found that while the total number of polymorphonuclear cells is increased in leukemia, their number in each 1000 leukocytes is really diminished; thus, in his 18 cases there were 49.2 per cent. of polymorphonuclear leukocytes and 7.6 per cent. of lymphocytes. The polymorphonuclear cells may be very small, and give an unusually dark-colored staining reaction; some may be pale; the shape of nuclei may be unusual. Neutrophilic granules may be fewer than normal. Sometimes the granules are entirely absent; rarely the protoplasm contains a few oxyphilic granules. The lymphocytes in Cabot's cases were diminished from the normal 20 to 30 per cent. to 7.6 per cent. Their absolute number per cubic millimeter was, however, always increased. The eosinophilic cell is also increased, but the proportion to other leukocytes may remain about normal. Cabot says there are three kinds of eosinophilic cells in leukemia—the ordinary, the dwarf, and the eosinophilic myelocytes. The last occur only in leukemia and occasionally in pernicious anemia. Basophilic cells are also sometimes found in leukemic blood.

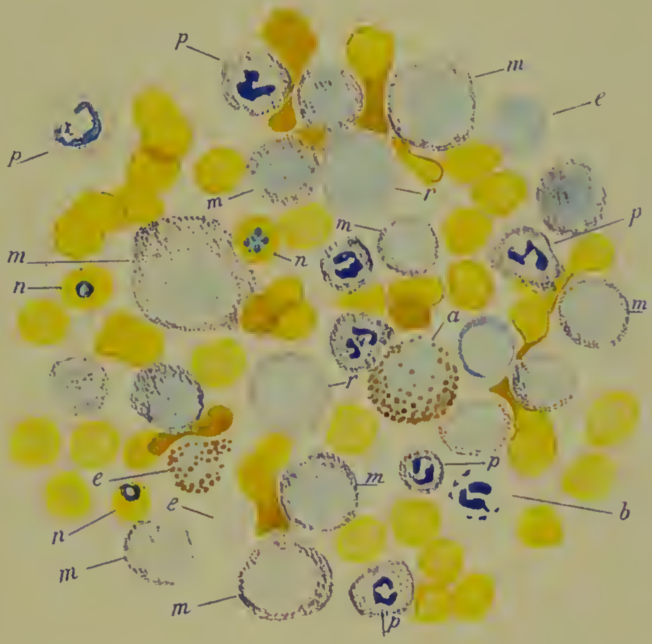

FIG. 233.—Myelogenous leukemia: *a*, Eosinophilic myelocytes; *b*, "mast-cell"; *e*, *e*, *e*, ordinary eosinophile; *m*, *m*, myelocytes; *n*, *n*, normoblasts; *p*, *p*, polynuclear neutrophiles; *r*, *r*, Reizungsformen (Türck) (cover-glass film stained with Ehrlich's "triacid" and drawn with camera lucida) (Cabot).

The blood changes can be studied during the life of the individual, and are such as to make diagnosis with the microscope readily possible. The specific gravity of the blood is generally diminished, and varies between 1.036 and 1.049. The alkalinity is somewhat diminished, and coagulation does not readily occur. The erythrocytes are reduced in number, averaging about 3,000,000 in ordinary cases. The hemoglobin is usually diminished, but the color-index is not particularly changed. Cabot studied 34 cases, in which there were 3,120,000 erythrocytes and 480,000 leukocytes on the average. Eichhorst has observed a case in which there were only 316,000 erythrocytes.

Sometimes large numbers of nucleated erythrocytes are present, the greatest number being present in the most serious cases; both normoblasts and megaloblasts may be found. The erythrocytes are said sometimes to show ameboid movement. In the so-called lymphatic form of the disease the red corpuscles are fewer than usual. Charcot-Leyden crystals may be found in the blood after death.

Stengel found the blood plaques strikingly increased in number. Prus found 2,000,000 per c.mm. It is curious and interesting to note that in leukemia the existence of an enormous number of leukocytes in the blood does not preclude the possibility of an accidental hyperleukocytosis when the proper conditions for its development arrive. Pfeiffer found the fibrin in leukemia to be less than that seen in hyperleukocytosis with fewer leukocytes in the blood.

According to the kind of cells found in the blood, which usually corresponds pretty accurately with the change in certain organs, it is customary to divide the leukemia clinically into two forms—the *splenomyelogenic*, characterized by changes in the spleen and bone-marrow and by the presence of myelocytes in the blood, and the *lymphatic*, characterized by changes in the lymphatic glands and in the occurrence of lymphocytes in the blood. The latter form is also called *lymphemia*.

LEUKEMIA.

Splenomyelogenic.		Lymphatic.
3,000,000 nucleated forms common	—Erythrocytes—	3,000,000, nucleated forms rare.
450,000, of which the myelocytes are 30 per cent.	—Leukocytes—	100,000 or less, of which the lymphocytes are 90 per cent. or over, myelocytes and eosinophiles few.

Pseudoleukemia of Infancy.—Von Jaksch has described a peculiar rare disease of early childhood under the name of anæmia infantum pseudoleukemica. It is characterized by marked anemia, hyperleukocytosis, and swelling of the spleen, liver, and glands. The condition is probably a secondary one whose nature has not yet been satisfactorily made out. It affects children under four years of age, probably being most frequent between the ages of seven and twelve months; male children suffer more frequently than those of the other sex.

The splenic enlargement, one of the cardinal symptoms, is so marked that at times the entire left side of the abdomen is occupied by a hard and firm splenic tumor. When the organ can be examined, it is found that the changes consist of a simple hyperplasia.

The liver, which is also frequently enlarged, shows no characteristic changes. The lymphatic glands are often enlarged, but never conspicuously so. The bone-marrow is soft and red.

The blood changes are characteristic, consisting in marked diminution of the erythrocytes and marked increase in the leukocytes. In one of von Jaksch's cases the erythrocytes were reduced to 820,000. Many of the erythrocytes appear to be degenerated and vacuolated. Polychromatophilia has been observed. Normoblasts are common; megaloblasts occasionally occur.

The leukocytes may increase so as to reach 1 to 12 red cells. The chief increase is in the polymorphonuclear cells, so that the condition is really more a hyperleukocytosis than a true leukemia. Occasionally the lymphocytes are also increased. The eosinophiles may be increased or diminished in number. The number of leukocytes varies from time to time.

The condition subjects the patient to marked danger from intercurrent affections, and is occasionally itself a cause of death from peritonitis, etc., though recovery usually follows.

Hodgkin's disease, pseudoleukemia (Cohnheim), or **general lymphadenoma** is not a disease of the blood, but a peculiar affection characterized by progressive hyperplasia of the lymphatic nodes, with anemia and occasional secondary lymphoid growths in the organs. It is mentioned because of the close clinical relationship which seems to exist between it and leukemia, which makes it natural to think of the two diseases at the same time, and because the disease is associated with anemia of some importance. It occurs most frequently in young males. Gowers found it most frequent between the twentieth and thirtieth and between the fiftieth and sixtieth years. Osler found 60 per cent. of the cases to occur in persons less than forty years of age. The cause of the disease is unknown. In the literature, malaria, scrofula, sarcoma, syphilis, rickets, and other diseases appear to be confused with Hodgkin's disease, and all have been mentioned as causes of it.

The morbid anatomy consists of an enlargement of the lymphatic nodes, usually affecting chains of nodes and causing them to become enormously enlarged, so that small nodes, such as are found in the cervical region, attain the size of the fist. The swellings are, hard and firm, but late in the course of the disease become elastic and fluctuate. When incised, the contents immediately project from the capsule, under considerable tension. The neighboring nodes frequently coalesce, and form enormous masses which sometimes rupture and invade the adjacent subcutaneous areolar tissue. When cut, the tumors are grayish or white in color, homogeneous, soft, and juicy. The glands occasionally suppurate. Those most frequently affected are in the neck, axilla, and mediastinum.

In the posterior mediastinum masses of enlarged glands may surround and press upon the aorta and trachea. The retroperitoneal glands are also affected, and may compress the abdominal viscera. Upon microscopic examination the tissue does not vary from the normal. The spleen is usually hypertrophied. On section, it is mottled from the presence of numerous islands of lymphoid tissues, and closely resembles the leukemic spleen. The liver may be enlarged from the presence of scattered lymphoid growths. The kidneys are commonly affected, their appearance being similar to that seen in leukemia. The marrow of the long bones is sometimes changed into a rich lymphadenoid tissue, such as has been described in leukemia. The lymphadenoid tissues are almost universally subject to enlargement and infiltration. In rare cases it is said that subcutaneous nodes soften and produce lesions similar to those of mycosis fungoides.

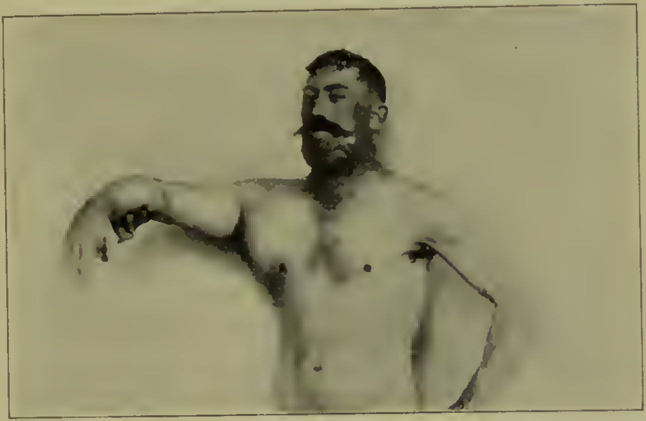

FIG. 234.—Hodgkin's disease, showing marked enlargement of the glands of the right axilla, with consequent dropsy of the arm; less marked involvement of the submaxillary and cervical lymph-glands (Stengel).

In the diseased tissues bacteria are frequently found, but no one species predominates, and those present can easily be accounted for as accidental or terminal infections. It is not likely than any of the bacteria thus far described in connection with the disease play any important etiologic rôle. The disease is usually fatal, though occasional recoveries are on record. The chief difference between Hodgkin's disease and leukemia resides in the fact that in the former the blood is comparatively normal, while in the latter the pathologic leukocytosis is characteristic. In pseudoleukemia the erythrocytes generally number about 4,000,000, though they may sink to 1,000,000; nucleated cells are unusual; there is rarely marked poikilocytosis. The leukocytes may be slightly increased in number, the highest number counted by Cabot being 64,000. The increase is chiefly in lymphocytes; the hemoglobin may be 30 per cent. or upward. A few cases are recorded in which pseudoleukemia is said to have changed into leukemia; such cases are, however, to be looked upon with suspicion, as there are numerous reasons why a mistake in diagnosis could be made.

THE SECONDARY ANEMIAS.

Symptomatic or secondary anemias can be adequately explained as depending upon such general or local conditions as may interfere with proper blood-formation, regeneration, or oxygenation, interference with digestion and nutrition, or loss of blood by hemorrhage or hemolysis.

Such conditions may depend upon:

1. Bad hygienic surroundings—
   - (*a*) Insufficient food or food of bad character.
   - (*b*) Inspiration of noxious gases.
   - (*c*) Overwork and crowding.
2. Parasitic diseases—Helminthiasis—Ankylostoma.
   - Bothriocephalus.
   - Teniæ.
   - Distoma.
   - Filaria.
3. Chronic exhausting disease—Cardiac disease.
   - Kidney disease.
   - Gastro-intestinal diseases.
   - Cirrhosis of the liver.
   - Rachitis.
   - Scorbutus.
4. Chronic infectious diseases—Tuberculosis.
   - Syphilis.
   - Leprosy.
   - Malaria.
5. Frequently repeated small losses of blood—
   - Menorrhagia.
   - Metrorrhagia.
   - Hemoptysis.
   - Epistaxis.
   - Hemophilia.
   - Scurvy.
   - Purpura.
   - Hemorrhoids.
6. Excessive physiologic strains—
   - Overlactation.
   - Gestation.
7. Toxemia—Saturnism.
   - Mercurialism.
   - Jaundice.

There is a loss of albumin from the plasma, so that the specific gravity is distinctly diminished. The alkalinity of the blood has been found increased.

The erythrocytes are diminished in number to a varying degree, according to the severity of the case. The reduction may be from a few hundred thousand corpuscles to millions, and it is not unusual to find patients with only 1,000,000 erythrocytes or even less. The corpuscles are altered in appearance according to the severity of the case. Usually the aberration from the normal is slight and scarcely noticeable, or, on the other hand, it may be so marked that a glance at the microscopic specimen will show abnormally pale or unusually small corpuscles. Nucleated corpuscles of the normoblast type sometimes occur. Megaloblasts occur only in the severe forms. Polychromatophilic corpuscles are met with, indicating that the condition is serious. Poikilocytosis is rare, and usually not marked.

The hemoglobin is diminished, the hemoglobin corpuscle ratio remaining about normal, though Stengel points out that, as a rule, the hemoglobin suffers a greater proportional reduction than the corpuscles. In tuberculosis, syphilis, rickets, carcinoma, etc., the blood condition may be identical with that of chlorosis.

The leukocytes are very variable in symptomatic anemia, sometimes being markedly increased in cases in which infection, hemorrhage, intoxication, etc., exist, and at others being normal or even decreased. In the malignant diseases lymphocytosis may occur.

Addison's Disease.—This affection is not a disease of the blood, but one whose principal lesions are situated in the adrenal bodies. Inasmuch, however, as disease of the adrenal bodies seems to be accompanied by a serious anemia, it is not improper to give it brief mention at this point. It may be defined as a pigmentary affection of the skin, forming a conspicuous symptom of an affection otherwise characterized by anemia, depressed circulation, indigestion, and asthenia. The disease affects men more often than women, and it most commonly develops between the twentieth and fortieth years. The chief lesion is in the suprarenal capsule. It seems to be immaterial just what the lesion is if the parenchyma of the glands be destroyed. Thus, it has been seen to follow atrophy of one or more glands, tuberculosis, which is the most common cause, carcinoma, and sarcoma. Other diseases of the glands, as, for example, amyloid, affecting the stroma and not the parenchyma of the organ, do not produce it. Addison was of the opinion that the disease depended upon loss of function of the adrenals, the blood gradually becoming poisoned by the retention of some material, the destruction or alteration of which is accomplished in these glands. The appearance of the diseased organs will, of course, vary with the disease which affects them. The skin of the patient is universally pigmented, the color usually being deeper on the exposed parts, varying from a light yellow to a deep brown or even black color. The discoloration is particularly striking to those who are not familiar with the negro and mulatto so common in this country. Here and there upon the surface leukoderma, or patches of atrophied pigment, may occur. The pigmentation also occurs upon the mucous membranes of the mouth, conjunctiva, and vagina. Occasionally the serous membranes are pigmented. The anemia is secondary and of rather moderate grade, though it may become severe.

Malaria.—Being a parasitic disease, the parasite of which is now well known, its consideration seems more naturally to find its place among the animal parasites than in the special pathology of the blood.

Purpura, Purpura hæmorrhagica, or **morbus maculosus Werlhofii,** is characterized by the occurrence of small purplish spots beneath the skin, and depends upon infectious and toxic conditions.

Banti's disease is a peculiar affection of unknown origin, characterized by splenomegaly, cirrhosis of the liver, and secondary anemia.

Polycythemic cyanosis is a little-understood affection, characterized by splenic enlargement, cyanosis, and polycythemia. The cause of the cyanosis is difficult to understand, and the polycythemia, which may amount to 9,000,000 erythrocytes per c.cm., equally unexplained.

CHAPTER II.

DISEASES OF THE CARDIOVASCULAR SYSTEM.

DISEASES OF THE HEART.

Congenital Malformations of the Heart.—Congenital absence of the heart is seen only in acardiac monsters (*q. v.*). The more usual malformations are structural deficiencies, and comprise—

1. Imperfect septa.
2. Anomalies of the arterial orifices.
3. Anomalies of the valves.
4. Persistence of fetal openings.
5. Transpositions.

These malformations are, in nearly all cases, explained by irregularities in embryonal development. The heart makes its first appearance in the embryo at a very early period, in the form of a straight undifferentiated tube, which drops into the cervical and still later into the thoracic region, at the same time making a peculiar sigmoid curve by which it becomes much shortened. A transverse constriction next separates the arterial and venous divisions into what later become the ventricles and auricles respectively.

The transformation of this simple heart, which resembles that of a fish, into the double mammalian heart is accomplished between the fourth and seventh weeks, by the growth of ridges upon the inner surfaces corresponding to grooves upon the outer surface.

The division of the auricles begins about the fourth week, but is not completed until after the ventricles are divided. The auricular septum is formed during the eighth week, but an opening, the *foramen ovale*, remains, and permits the blood to pass from the right auricle to the left until after birth.

The formation of the aorta and pulmonary artery takes place by division of the truncus arteriosus at the time the septum ventriculorum is completing its formation—about the seventh week.

From this brief review of the developmental stages it is evident that all serious cardiac malformations must occur during early embryonal life.

1. **Imperfect Septa.**—Should the septa fail to appear, the embryo has a simple heart, like that of a fish. If the ventricular septum fail to develop, the heart remains similar to that of the amphibians, with two auricles and one ventricle. Such defects may not be incompatible with embryonal development, but life after birth is impossible because of the inability of the individual to maintain his own circulation.

Incomplete development of the septa is more frequent, and may not interfere with post-uterine existence, according to the facility with which the arterial and the venous blood mix.

Imperfection of the auricular septum is common, the chief cause being *persistence of the foramen ovale.* Imperfect closure of this orifice is exceedingly common, but as the imperfection is usually well closed by the reduplication of endocardium springing from the *annulus ovalis*, it may never be recognized during life. If the persistent foramen ovale permits ready mixing of the aërated and non-aërated blood, it makes itself recognized at once by cyanosis. The well-known "blue baby" suffers from cyanosis depending upon this cause. The condition is incompatible with healthy existence.

2. **Abnormalities of the arterial orifices** depend upon irregular division of the *truncus arteriosus* at the time of the separation of the ventricles. Under normal conditions the division of the truncus arteriosus leads to the formation of two ostia of about equal size. Sometimes, however, the division is irregular, one of the orifices becoming, in consequence, smaller than normal—sometimes so narrow as to impede the circulation of the blood. The stenosis is usually at the pulmonary orifice, though sometimes at the aorta.

In rare cases the position of the vessels becomes transposed so that the aorta arises from the right ventricle and the pulmonary artery from the left.

When the division of the truncus arteriosus is extremely unequal, so that the establishment of circulation through the pulmonary artery is impossible, the septum ventriculorum remains defective and the aorta subtends both ventricles. The ductus arteriosus remains patulous, however, in these cases, and the blood from the ventricles, passing out through the aorta, goes in part to the arterial, in part to the pulmonary, circulation through the ductus arteriosus. Stenosis of the aorta at its origin may be compensated for by hypertrophy of the right ventricle, and the discharge of the systemic blood through the ductus arteriosus into the aorta beyond the stenosis.

3. **Abnormalities of the Valves.**—The auriculoventricular valves are not infrequently abnormal in length and adjustment, so that they imperfectly close the orifices. The *chordæ tendineæ* may also be too short and prevent the otherwise well-formed valves from closing. The aortic and pulmonary valves may be excessive or may be deficient in number. Valvular defects do not, however, interfere with the proper performance of the function of the heart, as they are usually compensated for by hypertrophic and other changes in the muscular structure of the heart.

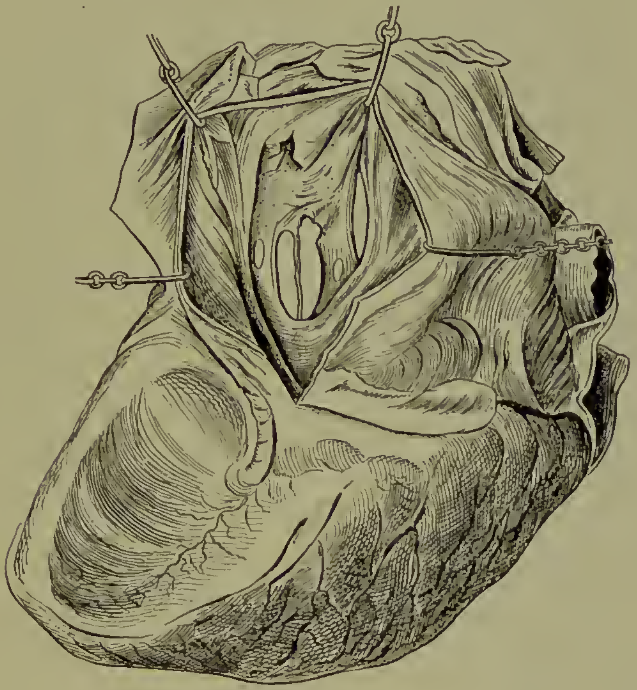

FIG. 235.—Defects in auricular septum, as seen from right auricle, which is laid open (after Musser).

4. **Persistence of Fetal Openings.**—Immediately after birth the necessity for the *foramen ovale* and *ductus arteriosus* disappears, as the direction of the circulation becomes changed through the development of the pulmonary circulation. These openings, therefore, immediately prepare to close and cease to exist a few days after birth. Should either of them fail to do so, however, the arterial and venous bloods are permitted to mix, to the physiologic detriment of the individual.

5. **Transposition of the great vessels,** the aorta arising from the right ventricle and the pulmonary artery from the left ventricle, is a very rare anomaly. In such cases the appearance of the whole heart is reversed, as the right ventricle becomes thick-walled, while the left remains thin. Other defects are usually present in such cases.

DISEASES OF THE PERICARDIUM.

There are but few recorded cases of malformation of the pericardium. In a few rare cases in which the heart was present the pericardium was also congenitally absent. It is absent in acardiac monsters. The relation of the pericardium to the heart is sometimes abnormal, the membrane is sometimes incomplete, and the heart may escape from the pericardium through defects in its structure.

Hyperemia.—Active hyperemia is usually preliminary to inflammation. Passive hyperemia occurs in cases of cardiac or other affections characterized by venous engorgement. The veins are unusually prominent, and in long-continued cases dilated. Passive hyperemia is not infrequently associated with non-inflammatory watery accumulations in the pericardium—*hydropericardium*.

Hemorrhage into the pericardium—*hematopericardium*—is not common. Subserous petechial or ecchymotic patches are sometimes met with in scurvy, purpura, and the infectious diseases. Actual bloody exudate sometimes characterizes cancerous and tuberculous inflammations. In traumatic lesions of the pericardium itself, and especially in cases of rupture of the heart, great vessels, or aneurysms, the pericardium may be full of blood.

Pericarditis.—Inflammation of the pericardium is the most important lesion.

Etiology of Pericarditis.—Cases whose cause cannot be determined are described as *idiopathic*. As we gain more complete knowledge of the subject, however, the number of primary idiopathic cases becomes smaller.

1. Primary pericarditis may be *idiopathic* or dependent upon undiscoverable causes; *traumatic*, depending upon injuries inflicted upon the pericardium directly, or *infectious*, and dependent upon bacteria which have entered from the intestine, the tonsils, or through insignificant lesions, and are accidentally brought to the pericardium. Primary inflammation of the pericardium also occurs in nephritis.

2. Secondary pericarditis is caused either by direct or by indirect infection of the pericardium from previously existing lesions. Thus, in rheumatism the micro-organisms in the blood commonly produce inflammation of the pericardium. Abscesses of the mediastinum, abscesses of the lung, tuberculous cavities of the lung, ulcerations of the stomach with fistulæ, diseases of the bronchial lymphatic glands, and a variety of other diseases of contiguous organs may cause invasion of the pericardium both directly by rupture into its cavity or indirectly by lymphogenous metastasis. The entrance of foreign bodies through the ruptured esophagus, etc., also produces suppurative pericarditis.

Morbid Anatomy.—Pericarditis is of variable severity, sometimes presenting itself in a mild form characterized at first by hyperemia and later by a serofibrinous exudate. According to the severity and duration of the disease, there may be only a moderate quantity of exudate (200–400 c.c.) or there may be as much as two liters. Alonzo Clarke has seen a case in which the pericardium was so distended as to contain four liters of seropurulent fluid. The serum may be clear and amber-colored, but usually is clouded from suspended flocculi of fibrin. The pericardium itself is thickened, slightly roughened, velvety where not covered with exudate, and coated with fibrin which may form either occasional flakes and granules or an even layer upon the surface, or, as is still more frequent, occur as an irregularly deposited, sticky accumulation. The movements of the heart have a good deal to do with the appearances. On the anterior surface, where the heart is only occasionally in contact with the pericardium, the movements of the heart roll the fibrin flakes into villus-like, rounded masses, while posteriorly and inferiorly, where the pressure of the heart is uniform and constant, the fibrin spreads out like a membrane, resembling the omentum. Considerable-sized exudates sometimes present the appearance described as "bread-and-butter pericardium," because of the mixed yellow-and-white appearance and the irregular surface which Laennec described as looking like approximated buttered surfaces quickly separated.

In still more marked cases the fibrinous exudate appears as cords and shaggy, coarse, woolly projections, making the surface of the heart appear hairy or villus (cor villosum).

In the course of time the serum is absorbed, the fibrin gradually disintegrates, the replacement of the exudate by newly formed connective tissue takes place, and the heart becomes united to the pericardium by firm fibrous tissue which resists its movements, and by making tension upon its valves, sometimes brings about subsequent hypertrophy, or fibrous cords which bind the cardiac and parietal pericardia together here and there, or, if the epicardium is chiefly affected, causes the heart to become more or less invested with a connective-tissue rind.

When organization is delayed and nutrition bad, deposition of lime-salts occurs in the inflammatory exudate, and concretions of greater or less magnitude are formed. These may exist simply as circumscribed thin deposits or may be so diffuse and extensive as to surround the heart by a stony encasement.

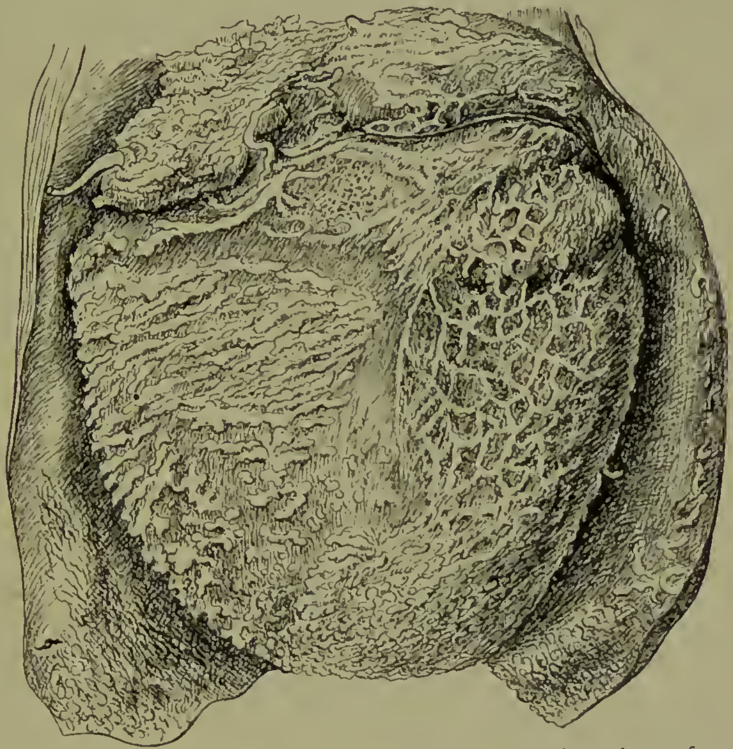

FIG. 236.—Fibrinous pericarditis; pericardium turned back to show the surface of the heart covered with fibrinous formation (Orth).

The entrance of infectious agents into the pericardium by external puncture, by the perforation of abscesses and tuberculous lesions of the lung, mediastinum, stomach, esophagus, etc., causes the formation of a purulent inflammation with *pyopericardium*. If the patient lives, the cycle of changes is identical with that of the simple serofibrinous inflammation unless the purulent collection be too great to be absorbed, when the pus will burrow and "point." The pointing and evacuation may be from some point in the neighborhood of the heart—usually at the base of the pericardium—but may be in the neck, in the back, or as low as the renal region. It may be mistaken for retroperitoneal abscess. If the pus remain and putrefactive bacteria enter, *pneumopericardium* is formed.

Pathologic Histology.—There is nothing peculiar about the microscopic appearance. There are more or less infiltration with round-cells, vascular dilatation, and disturbance of the endothelium, which is proliferated or destroyed. The free surface is thickly covered with a mass of fibrin, in part precipitated from the exudate and in part depending upon subendothelial fibrinous exudation or fibrinoid degeneration.

Pathologic Physiology.—Pericardial effusions cause marked embarrassment of the circulation by pressure upon the auricles and great veins. As described by Lazarus-Barlow, the mechanism of the embarrassment is as follows:

> "The increase of pressure in the pericardial sac is an obstacle to the inflow of blood into the heart, for normally the inflow of blood into the right auricle is greatly favored by the difference in pressure inside and outside the thorax, or, more strictly speaking, outside the thorax and inside the great veins at their entrance into the heart. Since the right auricle receives less blood than normal, it can pass on less blood to the right ventricle, the right ventricle in its turn ejecting less blood into the pulmonary artery; the pulmonary blood-pressure, therefore, falls. For the same reason—*i. e.*, because the pulmonary artery receives less blood than normal—less blood reaches the left auricle, and through it the left ventricle, by way of the pulmonary veins. Since the left ventricle receives less blood, its output into the aorta is diminished, and diminution of output of the left ventricle, unaccompanied as in this case by a corresponding increase in the peripheral resistance, is of necessity associated with fall of the aortic blood-pressure.
>
> "The venous blood-pressure, on the other hand, rises . . . because a new condition has been introduced into the circulation which disturbs the hitherto existing equilibrium between the inflow into and outflow from the heart. It is evident, since the aortic blood-pressure is dependent upon the two factors,—(*a*) output of the heart, and (*b*) peripheral resistance in the arteries, and since the output of the heart, *cæteris paribus*, depends entirely upon the inflow into the heart,—that, for the maintenance of a constant mean level of aortic blood-pressure, the inflow into the heart and the output must be exactly equal. But the blood which constitutes the 'inflow' is nothing more than that amount of blood which, as the result of hyperdistention, passes from the arteries into the veins during cardiac diastole. In other words, for the maintenance of a constant aortic blood-pressure the amount of blood which passes from arteries to veins during a given cardiac diastole must be exactly equal to the amount of blood which has been thrown into the arteries during the previous cardiac systole, and vice versâ.
>
> "In the case of a dog into whose pericardial sac oil is injected, the output of the heart is diminished, but since, at the moment before this occurred, the hyperdistention of the arteries corresponded to a greater output, the amount of blood which passed from arteries to veins also corresponded to that greater output. More blood, therefore, leaves the arterial system during any given diastole than enters it during the succeeding systole; an additional amount of blood, therefore, becomes stored up in the veins with each heart's diastole until equilibrium is once more established, gradually leading to the rise in venous pressure which we have noted. . . It is this rise of venous pressure which renders maintenance of the circulation possible under the altered conditions, for it is obvious that if the pericardial pressure were raised—to, say, 25 mm. of oil—while the pressure in the external jugular and other veins outside the thorax remained at their normal point, no blood would flow into the right auricle at all and the circulation would immediately cease. . . . As it is, however, the venous pressure rises with the intrapericardial pressure and always maintains a slight superiority; blood, therefore, flows into the right auricle, and though the pressures in arteries and veins are altered, the circulation goes on. . . . But the pressure which can be attained in the venous system has a limit which varies with many factors. . . . So long as the intrapericardial pressure is below (the extreme limit), the circulation continues, however poorly; but once the intrapericardial pressure reaches this point, all possibility of inflow from veins to auricles ceases and circulation comes to a standstill—the whole of the blood of the body collected in the veins. . . . The heart, however, in experimental cases, for a minute or thereabouts continues to contract, and if, during this time, the intrapericardial pressure be reduced, circulation reëstablishes itself. . . ."

The amount of fluid necessary to bring about the circulatory embarrassment described is not constant, and great difference exists in the rapidity with which the fluid accumulates. The rapid introduction of fluid into the pericardium in experimental study, and the sudden entrance of blood by rupture of the heart or of aneurysms, or of pus from evacuation of liver abscesses, hydatid cysts, etc., is rapidly fatal, though the actual quantity of fluid may not exceed 150 to 200 c.c., while the gradual collection of 1000 to 2000 c.c. of fluid in pericardial effusions may cause no other symptoms than cyanosis, because of the diminished amount of blood in the lungs and increased absorption of oxygen from the blood retained in the tissues, the difference being simply one of successful or unsuccessful equilibration of forces.

Milk Spot, or Friction Sclerosis.—Upon the inferior aspect of the right ventricle of the heart milk-white spots varying in size from a cent to a half-dollar, and made up of a thin layer of connective tissue deposited below the endothelial layer, are commonly seen. These are the so-called "milk spots" or "tendinous spots." At one time they were thought to indicate previous pericarditis, but now it is generally believed that they are caused by a process essentially chronic in nature, gradual in development, and in no way related to pericarditis as described. Whittaker prefers to call them "friction scleroses." In addition to the "milk spots," friction scleroses frequently appear as whitish lines along the course of the pericardial vessels.

Tuberculosis of the pericardium may be part of general miliary tuberculosis, or may, in very rare cases, depend upon the primary lodgment of tubercle bacilli in the pericardium. It is usually secondary to tuberculosis of the lungs, bronchi, and bronchial and mediastinal lymphatic nodes. Miliary tubercles are formed, except when the rupture of a cavity or of a softened bronchial node permits the escape of its contents into the pericardium, when pyopericardium is apt to result. Conglomerate and cheesy tubercles and masses sometimes form and are apt to be accompanied by sanguinolent or puriform collections in the cavity. In rare and well-marked cases the distribution of tubercles via the lymphatics of the pericardium leads to the ultimate formation of a universally thickened, nodular, roughened membrane, covering the heart and lining the pericardium, in which seropurulent fluid in small amount is present.

Syphilis, lepra, etc., usually produce no recognizable changes in the pericardium.

Actinomycosis rarely extends from the lung to the pericardium.

Tumors of the pericardium are usually secondary. *Endothelioma, fibroma,* and *lipoma* are rare primary tumors. *Sarcoma of the mediastinum* and *epithelioma of the esophagus and stomach* sometimes extend to the pericardium.

Parasites—cysticercus, echinococcus, and trichinæ—have been seen in the pericardium.

DISEASES OF THE MYOCARDIUM.

Cloudy swelling of the myocardium occurs in infectious and toxic conditions, such as the exanthematous fevers, phosphorus and arsenical poisoning, etc. It is apt to terminate in fatty degeneration.

The heart is enlarged, the muscular tissue grayish-yellow or grayish-red in color, and dull upon the cut surface. The consistence is somewhat friable. Microscopically, the cells present the granular appearance characteristic of albuminous degeneration. The transverse striations of the cells are indistinct.

Fatty metamorphosis of the heart muscle is a common and serious disease, which occurs in marasmatic, infectious, and toxic conditions. It may be quite uniform in distribution. When dependent upon local causes, such as the dissemination of groups of bacteria, alterations in the coronary circulation, etc., it may be focal and irregular. In extreme cases the heart may present a uniform yellowish or yellowish-gray color, and its consistence be soft, flabby, and lacerable. When cut, the blade of the knife becomes covered with oil, and drops of oil may be scraped from the surface.

From this extreme condition the lesion passes through all grades of severity until almost normal-appearing hearts are reached, in which one must look carefully for focal areas of necrosis in the papillary muscles, musculi pectinati, etc., beneath the transparent endocardium. One of the most characteristic appearances is yellowish mottling on the dark background of the red muscle. A very marked "tabby mottling" is seen in pernicious anemia.

The affected muscle-cells contain minute fat-granules, the transverse striations are absent, and retrogressive changes are observed in the muscle nuclei. In many cases the lesion can be recognized only by microscopic examination. The fat-droplets in the cells may be few or many, but usually remain small and do not coalesce to form drops.

Fatty metamorphosis is always an important and serious change that diminishes the contractile power of the cells, predisposes to stretching of the muscle, with dilatation, and may lead to rupture of the heart, from its inability to resist the internal pressure of the blood. It is a common cause of acute dilatation and death.

Fatty infiltration is scarcely a disease of the myocardium, though it brings about its partial disappearance. The infiltration of fat takes place in the subepicardial connective tissue, where a certain amount of it is normal, and then spreads along the intermuscular tissue, infiltrating cell after cell, and causing pressure atrophy of the muscle tissue. It chiefly affects the left ventricle. The depth to which the infiltrated tissue may extend is sometimes so great that the fatty tissue can be recognized from the inner surface of the right ventricle. The condition is properly described as *obesitas cordis*.

Amyloid disease of the heart is unusual, and more often irregular than uniform in its distribution. It occurs in the subepicardial and intermuscular connective tissues.

Necrosis or **myomalacia cordis** is necrotic softening of the cardiac muscle, from which disease or accident has withheld the circulation. Its most common cause is sclerosis of the coronary arteries. It may also result from thrombosis, embolism, or senile calcification of the coronary arteries.

The most common seat of disease is the anterior or posterior wall of the left ventricle, near the apex; it may, however, occur anywhere in the muscular structure of the heart—not infrequently in the papillary muscles. The condition may be recognized in the beginning by the dull yellow color of the affected area. Later this appears yellowish-white, and the tissue becomes mushy or lacerable. Its surface is depressed below that of the surrounding healthy tissue. When examined microscopically, it is found that the cells have lost their transverse striations and nuclei. When the condition depends upon embolism, hemorrhagic infarction may precede it.

If the affected area is large and extends through the entire thickness of the ventricular wall, rupture of the heart at the weakened point and fatal hemorrhage may occur.

If, on the other hand, the ventricle is able to withstand the blood-pressure, the softening of the necrotic tissue is followed by absorption of a part of the mass, while a reactive inflammation occurs around it, granulation tissue is formed and extends into it, and in the course of time the entire necrotic area is replaced by cicatricial tissue. As the cicatrix diminishes in size by contraction it recedes from the surface of the heart and leaves a pucker or dimple, at which point the heart-wall is much thinned and fibrous.

The cicatrix sometimes includes branches of the coronary arteries, compresses them, and predisposes to similar changes in other parts of the heart.

When considerable muscular tissue is thus destroyed and replaced by non-contractile connective tissue, the pressure of the contained blood during contraction acts with distending force upon the inelastic cicatrix and causes it to bulge more and more until a pocket-like dilatation or *cardiac aneurysm* is formed.

When the necrosis is subendocardial and the endothelium destroyed, a fibrinous deposit forms, augmenting in size until a form of cardiac thrombus known as a *cardiac polypus* is produced.

Brown atrophy of the heart muscle is a condition seen in senility and in constitutional diseases associated with profound anemia and cachexia. The heart is diminished in size and brownish-red in color. The condition may not be recognizable by the naked eye. When examined microscopically, numerous small brownish granules of pigment are found within the muscle-cells, usually clustered about the poles of their nuclei. It is sometimes difficult to differentiate them from fat, and the use of reagents may be necessary for the purpose. The transverse striations are less distinct than normal. Brown atrophy is not infrequently associated with fatty degeneration of the muscular tissue, both depending upon malnutrition.

Fibroid heart or **fibrous myocarditis** is, for the most part, a more or less circumscribed process that results from chronic endocarditis with fibrosis of the valves, coni arteriosi, chordæ tendineæ, papillary muscles, etc., from the healing of areas of myomalacia cordis, abscess, gumma, etc. More widespread fibroid changes may, however, succeed myodegenerations occurring in the course of the infective fevers, chronic passive congestion of the heart, and chronic pericarditis.

The heart, according to the extent of the disease, may or may not be enlarged. The connective tissue between the muscular layers and between the muscular bundles is increased, the increase usually being associated with atrophy of the muscular tissue and fatty degeneration of the cells in the immediate vicinity.

As the fibroconnective tissue is neither elastic nor contractile, its increase at the expense of the muscular tissue is extremely disadvantageous, and constitutes one of the most serious cardiac conditions.

Segmentation of the myocardium is a separation of the component muscle-cells. It is a common condition, usually preceded by abnormal distinctness of the cement lines between the segments.

Fragmentation of the myocardium is rupture of the muscle-cells, sometimes near the cement lines, but more frequently near the center. It is also an exceedingly common condition, occurring in upward of 50 per cent. of adult hearts examined.

In summarizing a very comprehensive literary and experimental study of the subject Hektoen says: "The cardiac muscle-fibers frequently separate into muscle-cells and irregular fragments. Segmentation and fragmentation are due to disproportion between the vigor and order of muscular contraction and muscular cohesion. They occur in normal heart muscle due to excessive vigorous and irregular contractions. More frequently they are encountered in association with acute and chronic, secondary and primary, myocardial changes that alter the cement, weaken the plasma, and predispose to dissociation under normal or increased heart's action.

"General segmentation is of brief duration, because its occurrence is incompatible with further cardiac contractions. Focal or limited segmentation may, perhaps, cause incompetency of the auriculoventricular valves, especially the mitral. It may lead to cardiac insufficiency, and possibly to rupture of the heart. The fate of the loosened muscle-cells is not known. It seems, however, that focal dissociation is of but short antemortem duration. The occurrence of primary segmentation as a distinct disease is not proven."

Both changes are most frequently observed in the left papillary muscle and interventricular septum. There is considerable evidence in favor of regarding both segmentation and fragmentation of the heart muscle as artefacts.

DISEASES OF THE ENDOCARDIUM.

Diseases of the endocardium are commonly called *endocarditis*, regardless of their true inflammatory nature. Though any part of the endocardium may be affected, the lesions are most marked upon its valvular reduplications.

It is customary to divide endocarditis into three forms: the *verrucose*, the *malignant* or *ulcerative*, and the *chronic* or *sclerotic*. As, however, the distinction between the verrucose and ulcerative forms is probably only one of degree, it is rather better to consider only two distinct forms—the *acute* and *chronic endocarditis*.

Acute endocarditis is an acute disease of the valves of the heart, infectious in nature, and characterized by the formation of warty growths and ulcerations by which the integrity of the valves may be destroyed.

Etiology.—It is now universally conceded that acute endocarditis is a secondary affection which occurs in the course of many micro-organismal diseases. It is most common in rheumatism, next most common in pneumonia, septic pyemia, and tuberculosis, but has been seen in nearly all the infectious diseases — puerperal fever, osteomyelitis, periostitis, erysipelas, furunculosis, dysentery, anthrax, suppurations of various internal and external organs, gonorrhea, scarlatina, variola, measles, diphtheria, typhoid, pericarditis, catarrhal pneumonia, influenza, syphilis, Bright's disease, and malaria. It has also been seen occasionally in some most trivial affections, such as quinsy and mumps.

Bacteriology.—That micro-organisms are the cause of the affection there is no longer room for doubt, as they are readily cultivated from the lesions. There is no specific bacterium causing endocarditis, but many varieties can be found. Of the species that have been cultivated may be mentioned Staphylococcus pyogenes aureus, Staphylococcus albus, Streptococcus pyogenes, Micrococcus lanceolatus, Bacillus coli communis, Micrococcus endocarditidis (of Weichselbaum), Bacillus fœtidus (of Fränkel and Sanger), the gonococcus, and the tubercle bacillus.

Morbid Anatomy.—The lesions of endocarditis are rarely found upon that part of the endocardium which covers the muscular substance of the heart (*mural endocarditis*), but are almost invariably located upon the valves (*valvular endocarditis*).

Any or all the valves may be affected, but the disease most frequently affects the mitral and aortic valves, except in fetal life.

"In 300 cases of endocarditis studied at the Pathological Laboratory of Berlin, 297 were on the left side and 32 on the right side; 268 were confined to the left side alone, and 3 to the right side alone."

The disease gives its earliest manifestations near the edges of the valves, *at the surfaces of contact*. One should be aware that there are sometimes slight defects of structure to be found in connection with the valves, which may be mistaken for the lesions of the endocarditis. Thus, in the hearts of infants it is not unusual to find small projections from the valves, composed of mucous tissue not yet absorbed, but bearing a partial resemblance to the warts found in endocarditis, and in adults thickenings resembling a hem at the edge of the mitral valve, depending upon irregular union of the two layers of endocardium forming the valve, are sometimes observed. Not rarely there are structural defects in the delicate valvular tissue in the form of small fenestra.

Endocarditis probably occurs in consequence of a slight alteration in the endothelial cells, which, because of the circulating toxic products of disease, undergo changes similar to those seen in the capillaries and lymphatics under similar stimulation, the cells tending to become spherical or fusiform in shape. This leaves abnormally large crevices between them, and affords an opportunity for the direct implantation of any bacteria circulating in the blood. Once in such a nidus, the bacteria produce more or less serious changes according to their biologic peculiarities; or it may be that the infection of the valve is indirect, the bacteria reaching its tissue through the coronary circulation, in support of which it must be pointed out that the lesions do not form at the edges of the valves when there are no capillaries, but at the lines of contact, to which capillaries extend.

In rheumatism and pneumonia, which are the most common causes of the disease, the changes are of a comparatively mild type. In the immediate neighborhood of the invading micro-organisms there is necrosis of the valvular tissue, whose endothelial cells and deeper connective-tissue cells change into a hyaline mass. Beyond this an infiltration of the tissue by small round-cells usually occurs in the valvular structure. Fibrin is deposited upon the abnormal surface of the valve, layer by layer, sometimes including some erythrocytes and leukocytes, until a small warty excrescence is formed at each invaded point. This form is known as *verrucose*, *polypose*, or *villous endocarditis*, according to the size and appearance presented by the projections upon the valves.

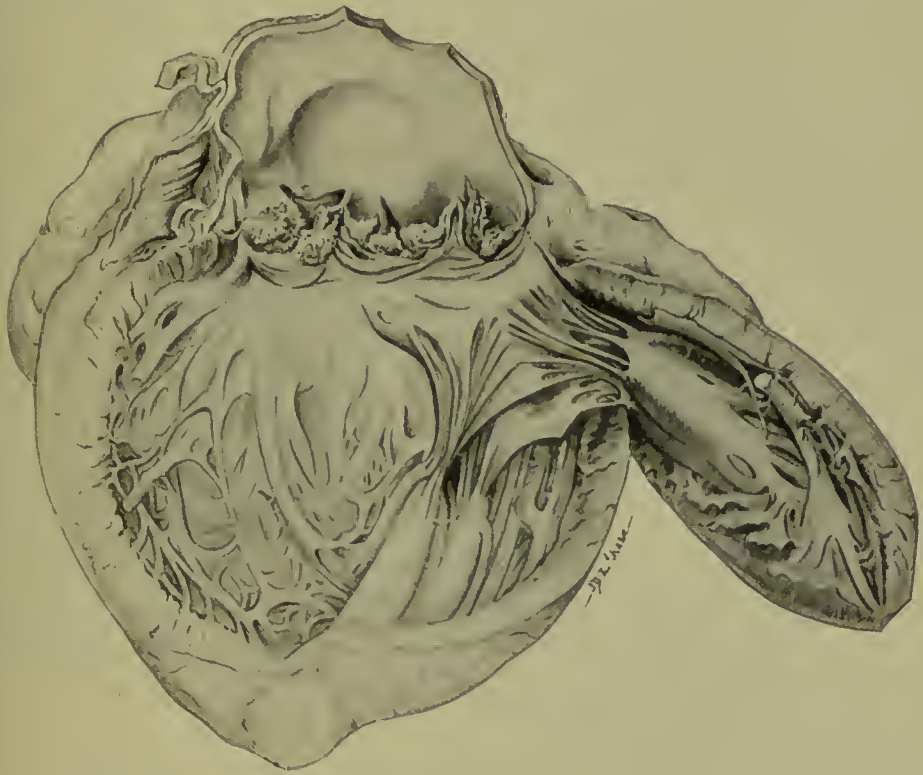

FIG. 237.—Chronic verrucose endocarditis of the aortic valves, showing the warty projections from their edges. The valves are at the same time thickened and stiffened by sclerotic changes.

The verrucosities are not infrequently torn loose by the passing bloodstream, causing embolism, while small, denuded, sometimes suppurating, ulcers remain. Cases in which numerous such lesions have formed are described as *pustular endocarditis*.

Combinations of verrucose, polypoid, villous, and pustular lesions can occur upon the same valve, representing different conditions caused by the infectious agents. The condition persists for a longer or shorter time, and then gradually passes into a chronic condition in which reparative changes take place, and the warty excrescences are replaced by permanent connective tissue, and the valves reinforced. These changes will be more fully discussed in speaking of *chronic endocarditis.*

When the disease is caused by more virulent micro-organisms, the changes are correspondingly more destructive and the condition is described as *ulcerative* or *malignant endocarditis.* In this form of the disease the avascular tissue of the valve slowly melts away before the invading bacteria. In the deeper parts of the valve the layers of endocardium may be separated by intermediate purulent collections, which later evacuate and leave extensive ulcerations upon one or the other valvular surface. The normal vessels of the valve dilate, and new vessels are formed. There is a slow attempt at organization, but instead of having smooth borders, the lesions almost invariably heal with irregular villous prolongations, consisting of granulation tissue, with more or less superimposed fibrin. These may later be torn loose by the passing blood and bring about infectious embolism of remote organs.

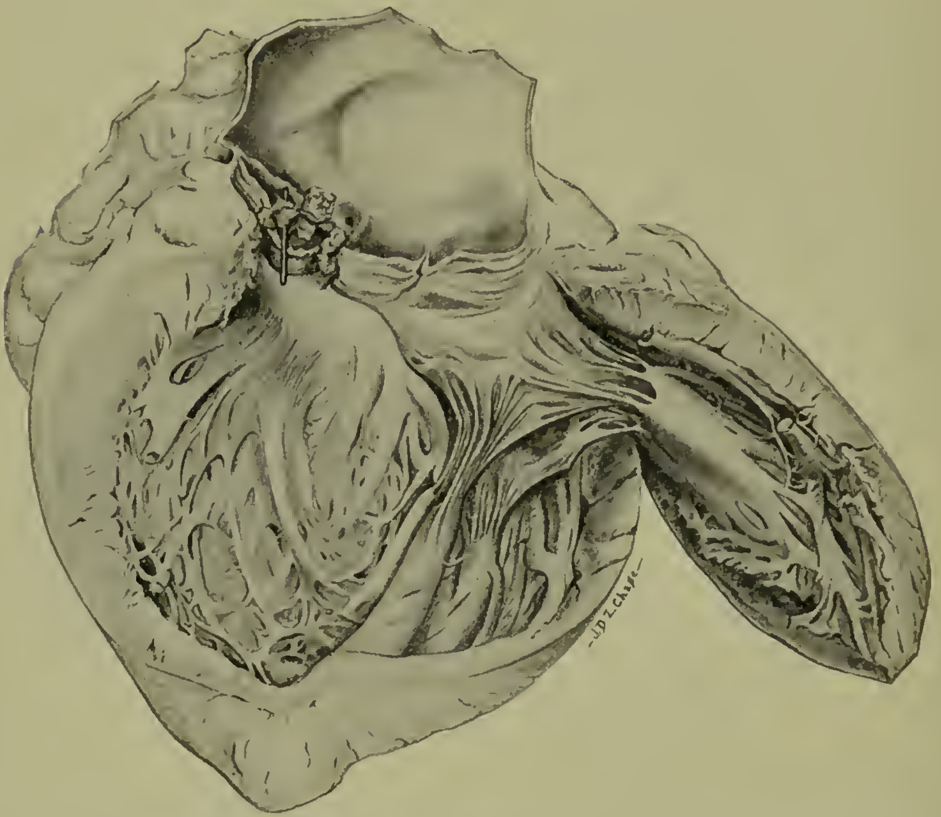

FIG. 238.—Malignant endocarditis of an aortic valve, showing villous projections and ulcerations. A small stick is introduced into a fenestration in the valve.

It is not unusual for the loss of tissue from combined necrosis and suppuration to bring about perforations of the valves,—*fenestration,*—so that they are no longer *competent* to withstand the backward flow of the blood, and when the fenestra are large and the destruction is progressive, the valve may remain attached to the heart by a single slender pedicle which itself may later be broken and permit the valve itself to enter the circulation as an embolus. The congenital fenestrations are readily differentiated from those of endocarditis by the absence of inflammatory thickening and induration.

When the valvular destruction has not extended so far, one surface may be eroded and weakened, so that it yields to the pressure of the blood after closure, and allows the formation of a pouch called an *acute valvular aneurysm*. A case has been reported in which a warty excrescence, attached by a thread of endocardium torn from the edge of the aortic valve, accidentally entered one of the coronary arteries, plugging it and causing almost instant death, with symptoms resembling angina pectoris.

Ulcerative endocarditis, being infectious, does not remain localized upon the valve, but produces lesions in the conus arteriosus, the contiguous myocardium, and part of the aorta as well. These all show purulent, degenerative, or proliferative changes.

Sclerotic endocarditis or **chronic endocarditis** is a chronic, progressive, sclerotic affection of the valves of the heart, characterized by thickening, stiffening, calcification, and incompetency of the valves. It sometimes, perhaps usually, succeeds acute endocarditis. It may, however, occur as an independent affection, essentially chronic, progressively destructive, and ultimately fatal.

It is characterized by sclerosis and mineralization. When the inflammatory phenomena of endocarditis have subsided, the process of repair begins. Cicatrization of the denuded surfaces takes place, the warty excrescences are sometimes made permanent by connective-tissue proliferation, and the infiltrated portions of the valve become thickened. In this manner the acute endocarditis recovers, but leaves behind it permanent alterations of the valves which exert a marked deleterious influence upon the circulatory function. The thickening detracts from their elasticity and stiffens them, so that they neither close easily to prevent the regurgitation of the blood, nor open readily to permit its outflow, and the projections from their edges offer resistance to the streaming blood (obstruction).

Contractions of cicatricial bands, and especially thickening and shortening of the *chordæ tendineæ*, prevent the proper closure of the valves (regurgitation). Calcification of the poorly nourished, newly formed tissue is very common.

In cases that originate *per se* the appearances are different because there have been no preceding destructive valvular lesions.

Primary sclerotic endocarditis receives its name in consequence of the proliferative changes, which resemble those seen in the repair of inflammations. The disease is probably more correctly spoken of as fibrosis.

Etiology.—Many cases depend upon local disturbances of nutrition and resemble "atheroma" of the blood vessels. It is essentially a disease of old age. Excessive physical strain, acting as a trauma of the valves, may predispose to sclerotic changes. Heredity seems to play a part in the etiology of the affection, and alcoholism, gout, chronic rheumatism, and various other disorders indicative of general bad nutrition or followed by fibrosis and arteriosclerosis are associated with it. Syphilis is also a probable cause, and, like alcohol, can be blamed for most of the sclerotic changes.

Morbid Anatomy.—The essential lesions of sclerotic endocarditis are two—fibroid induration and calcification. The valvular leaflets are slowly and insidiously invaded by a progressive deposit of fibroconnective tissue, which takes away their elasticity, produces a striking opacity, and gradually transforms them into thickened, inelastic, irregular, badly fitting barriers with curled, thickened, and rounded edges that sometimes remain competent to maintain the integrity of the circulation, though they more often fail to do so. The valves are not the only tissues involved, as it is common to see the chorda tendineæ thickened and shortened, pulling upon the valves so as to prevent their closure, and not infrequently the conus arteriosus so involved that the contraction of the connective tissue reduces the size of its outlet to a considerable extent.

Mineralization of the fibroid and indurated structure is frequent. When the destructive process common in the vessels—*atheroma* (*q. v.*)—takes place upon the valves, which is not rare, the mineral matter is deposited beneath the endocardium in the form of flattened plates, which may project from the surface of the valve like fish-scales. When the mineralization occurs in the deeper tissues, the entire valve may be so altered in texture as to be immovable, brittle, and mineralized, its appearance being less altered than its texture. The highest degree of mineralization probably occurs in the aortic valves.

Sometimes, but probably only in cases in which acute endocarditis has denuded the valvular leaflets of their endothelium, the segments unite, and one finds such anomalies as two aortic leaflets instead of three, etc. Careful examination will usually make clear the mode of formation, but the extent of the deformity may be such that in the narrowed, elongated conus the partially united valves may close the opening, with the exception of a central slit through which a lead-pencil will scarcely pass ("button-hole" orifice).

Marked stenosis of the conus arteriosus is probably more marked after prenatal endocarditis.

As the sclerosis progresses, the muscular tissue becomes more or less affected, atrophies, and is replaced by fibrous tissue. Hyaline degeneration of the fibers is common, amyloid disease of the muscular tissue is said to occur, and round-cell infiltrations scattered here and there throughout the muscle-cells are quite common.

Hypertrophy of the ventricles usually occurs to compensate for the valvular defects, and may in turn be followed by dilatation.

Mural endocarditis, or inflammation of the endocardium covering the muscular walls of the heart, is not common, though seen in acute endocarditis. It may occur in consequence of myocardial abscesses, gummata, or tuberculous lesions of the myocardium extending to the endocardium. Fibrin deposits upon the diseased surface, and protects it from the streaming blood until cicatricial changes can be completed.

After cicatrization a callous spot remains upon the inner wall of the ventricle.

In *atheroma* the ventricular endocardium is also sometimes involved, but only in extremely rare cases without conspicuous alteration of the valves.

VALVULAR INCOMPETENCE—INSUFFICIENCY AND STENOSIS.

In nearly all cases valvular incompetence results from endocarditis. It may, however, depend upon violent muscular exertions, which so increase the blood-pressure as to cause traumatic injury or aneurysmal dilatation of the valves and upon neoplasms or polypoid excrescences which interfere with their proper movements.

Valvular incompetence either permits the regurgitation of blood into the cavity of the heart through an imperfectly guarded orifice, or prevents the escape of the blood through a contracted opening. **Insufficiency with regurgitation** results from fenestration, rupture, and ulceration of the valves, adhesion of the valves to the wall of the heart, stiffening, calcification, and fibroid induration of the valves, so that closure is impossible. **Obstruction or stenosis**, on the other hand, occurs when polypoid or villous verruca form upon the edges of the valves; when valvular leaflets have united by inflammatory connective tissue; when fibroid induration has narrowed the ventricular ostium, or when marked calcification has made the valves immovable. In either case the function of the heart is embarrassed. The extent to which the embarrassment of the circulation may progress will depend in part upon the particular valve affected and the age and vitality of the patient and his ability properly to *compensate by hypertrophy*, etc., for the damage done.

CARDIAC HYPERTROPHY.

Cardiac hypertrophy is enlargement of the heart depending upon increase of its muscular tissue. It is both simple and numerical, the number and size of the muscle-cells being increased.

Etiology.—It has but one immediate cause—overwork.

1. **Resistance to the Action of the Heart.**—1. EXTRINSIC RESISTANCE TO THE MOVEMENTS OF THE HEART.—(*a*) The action of the heart is greatly impeded in *pericarditis* with adhesions. It is in cases of this kind that some of the largest hearts are seen.

(*b*) Displacement of the heart by *morbid growths*, aneurysms, empyemas, etc., increases its work and causes it to hypertrophy.

2. INTRINSIC RESISTANCE TO THE MOVEMENTS OF THE HEART.—(*a*) *Valvular lesions* with insufficiency and obstruction require that the strength of the heart's action be increased to compensate for the impediment. The enlargement of the heart in these cases is usually greatest in the parts immediately involved. It is, however, unusual to find hypertrophy of a single chamber, because it is almost impossible for increased blood-pressure to be exerted within one chamber of the heart without in some measure affecting the others.

The best illustration of this is probably seen in the most common valvular lesion, mitral regurgitation. In this affection, when the left ventricle contracts, all the blood does not escape from its cavity into the aorta, but some of it returns to the left auricle, which, under the constant unusual pressure, is obliged to offer increased resistance, which it does by increasing the amount of its muscular structure—hypertrophy. The increased auricular pressure occasioned by the return of blood from the ventricle causes obstruction of the pulmonary veins and capillaries, from which the blood fails to escape into the pulmonary veins, and compels a secondary hypertrophy of the right ventricle in order that the blood may be more forcibly driven from them into the left auricle.

The compensatory hypertrophy brought about in this way may cause the thickness of the right ventricle to equal or even exceed that of the left. When extremely hypertrophied, the right ventricle may form the apex of the heart.

Hypertrophy of the left ventricle usually occurs in consequence of disease at the aortic valve. In aortic insufficiency with regurgitation the heart may become enormous, meriting the term *cor bovinum*, sometimes applied to such hearts.

(*b*) The presence of cardiac *thrombi*, cardiac aneurysms, morbid growths, congenital defects, etc., all predispose to hypertrophy of the heart by increasing its work.

3. CONTRACTION AND RIGIDITY OF THE ARTERIAL SYSTEM.—*Increased resistance* in the peripheral circulation from abnormalities of the blood vessels increases the work of the heart and compels it to hypertrophy. The most common cause of this resistance is *arteriosclerosis*, but there are cases on record in which congenital contractions of the arterial system and abnormal narrowness of the aorta have coexisted.

Violent physical exertion seems to interfere with the cardiac action and lead to hypertrophy. This may depend in part upon the difficulty of driving the circulating blood through rapidly and violently contracting muscles, as well as in the unusual demands for nutrition made necessary by the increased work. Athletes of all kinds experience enlargement of the heart.

The hypertrophy of left ventricle that accompanies Bright's disease of the kidneys depends upon excessive stimulation of the heart by noxious products retained in the circulation, as well as upon the arterial constriction resulting from the same cause.

Diseases of the lungs, such as emphysema, by causing obliteration of many capillaries and compression of the remainder by the distended air-cells, increase the work of the right ventricle and cause its hypertrophy.

II. **Abnormal innervation** of the heart is a not infrequent cause of hypertrophy. The hypertrophy, under these circumstances, is rarely considerable, and is likely to be more symmetric than when depending upon obstruction. Irritation of the vagus nerve, such as occurs in certain pathologic conditions of the medulla or in irritations in the peripheral nerve by tumors, etc., may lead to cardiac hypertrophy. Exophthalmic goiter is almost constantly associated with enlargement of the heart, presumably depending upon its overstimulation by the accumulated products of the gland.

The excessive use of tobacco, coffee, and other cardiac stimulants by persons susceptible to their effects may also cause enlargement of the heart.

Morbid Anatomy.—The hypertrophied heart is abnormally large and heavy. From the normal 250 to 280 grams, the weight may run up to 1600 grams. The symmetry of the organ is disturbed. Hypertrophy of the left ventricle increases the length of the heart; hypertrophy of the right ventricle, its breadth. The auricles, when hypertrophied, are probably always dilated as well, and appear unusually large and prominent. The thickness of the ventricular wall is always greatest near the base, thinning toward the apex. Indeed, in some cases this thinning at the apex, while probably not abnormal, contrasts so markedly with the thickness near the base as to suggest that rupture at the apex during the powerful contractions would be an easy accident. It is, however, unknown, probably because of the direction of the muscular movements.

One must be cautious in pronouncing judgment upon hearts which have ceased to act in systole and are in rigor mortis. Osler recommends that they be soaked in water, thoroughly relaxed, and then measured. Thickness beyond 20 to 25 mm. indicates hypertrophy of the left ventricle; beyond 4 to 7 mm., hypertrophy of the right ventricle.

The muscular substance of the hypertrophied heart is dark red in color and firm in texture. It cuts with resistance.

The hypertrophy is not limited to any particular part of the muscular structure, but in the affected chambers involves all the columnæ carneæ, musculi papillares, musculi pectinati, etc. The following forms of hypertrophy are described:

I. *Concentric hypertrophy*, in which the ventricular wall is thickened at the expense of its capacity, which is diminished. This must be exceedingly rare.

II. *Simple hypertrophy*, in which the ventricular wall is thickened without any apparent change in the capacity.

III. *Eccentric hypertrophy* or *hypertrophic dilatation*, in which the ventricular capacity is increased and the ventricular walls are hypertrophied. This is the most common condition.

So long as a hypertrophied heart is competent to carry on its function without producing symptoms indicative of circulatory disturbance, it is said to be a *sufficient hypertrophy*. *Insufficient hypertrophy* signifies either that the heart has been unable to hypertrophy sufficiently to overcome its embarrassment, or, having done so, has subsequently failed. The most common outcome of this *insufficiency* or *lost compensation* is *dilatation*.

The **results** of cardiac hypertrophy may be serious. An overstimulated hypertrophied heart may cause so great an increase of blood-pressure as to occasion rupture of the aorta and death, or so increase the arterial pressure as to injure the vessels and capillaries, especially in the kidney, and thus cause secondary changes in the organs. It also predisposes to arteriosclerosis and apoplexy.

CARDIAC DILATATION.

Cardiac dilatation is an increase in the size of the heart, which depends upon the stretching and yielding of the muscular walls.

The condition may be *acute* and without previous appreciable disease of the organ, or, as is much more often the case, *chronic*, succeeding hypertrophy. On this account dilated hearts may have abnormally thick or abnormally thin walls.

Etiology.—There are two immediate causes of dilatation: (1) *Failure of the nutrition of the cardiac walls;* (2) *increased endocardial blood-pressure.*

The failure of nutrition is probably the most frequent cause of dilatation in hypertrophied hearts, the integrity of whose tissue depends upon a compensatory increase of nutrition. The capacity of the coronary arteries not being unlimited, the heart cannot increase in bulk indefinitely, for a time must come when the muscle will demand more nourishment than it can receive, and, failing to get it, will begin to degenerate. In nearly all cases the very cause that occasions the enlargement of the heart—endocarditis with subsequent sclerosis—affects the orifices of the coronary arteries and diminishes their caliber, gradually shutting off the blood-supply of the heart when it is most needed.

Sudden acute dilatation is sometimes seen in typhoid and other low febrile conditions associated with general malnutrition, and after excessive muscular efforts performed by those in somewhat poor physical condition.

Morbid Anatomy.—The heart is enlarged, soft, flabby, and full of blood. The dilatation is more often in the right than in the left ventricle, and more frequently in the left than in the right auricle. The most extreme degree of dilatation is probably seen in aortic insufficiency. In mitral stenosis the left auricle suffers most, and may be dilated to several times its normal size, while at the same time the right chambers of the heart are also dilated. It is usual to find several cavities similarly affected and distended with blood.

When the heart is opened, the large size of its cavities and the flaccid condition of its muscle are conspicuous. The walls may be thin or thick, according to circumstances, and the existence of dilatation must be judged by the size of the cavities. The auriculoventricular orifices are much enlarged and relaxed, and the valves show undoubted evidence of having been incompetent. The muscular substance may show marked fatty degeneration in acute cases, moderate degeneration in chronic cases.

If one ventricle is considerably dilated, the septum ventriculorum may encroach upon the other.

Pathologic Histology.—When the cardiac walls are examined, it is found that marked cellular changes are present. The endocardium is apt to appear clouded or opaque, particularly in the auricles, and the muscle is apt to show signs of fatty degeneration. It may be uniformly yellowish in color, or show irregular yellowish streaks or mottlings.

When examined microscopically, one finds fatty metamorphosis of the muscular substance the most frequent pathologic change.

CARDIAC ATROPHY.

Atrophy of the heart is not uncommon. It occurs chiefly in marasmatic conditions, such as senility, chlorosis, phthisis, starvation, passive congestion with increase of the intermuscular connective tissue of the organ, and in cases of pericarditis in which the heart is pressed upon by dense pericardial connective-tissue bands. Amyloid disease of the kidneys is also mentioned as a cause. Cases are on record in which the heart is said to have been reduced to one-half its normal size.

When examined, the atrophied heart is found to be smaller than normal, pale, or dark brown (brown atrophy, *q. v.*), flabby, and relaxed. It may at times present what is described as a "withered-apple" appearance, when the epicardium is thrown into wrinkles upon its surface.

The fatty tissue of the subepicardium is absorbed, the disappearance of the fat being associated with the appearance of some mucous tissue. The vessels upon the surface of the heart, on account of the retraction of the diminished tissue, appear to be abnormally serpentine.

PATHOLOGIC PHYSIOLOGY OF THE CARDIAC DISEASES.

It is erroneous to conceive of the different cardiac lesions as independent entities. Every important lesion of any part sooner or later occasions embarrassment of the whole heart. Disease of the pericardium or endocardium leads to fibroid and atrophic changes of the myocardium, by which its expansile and contractile powers are diminished. Disease of a valve is compensated for by hypertrophy of the wall of a chamber, which in its turn disturbs the circulatory equilibrium of the whole system and at the same time demands a local increased nutrient supply. Disease of the coronary arteries, by diminishing their caliber, predisposing to thrombosis, or in any other manner diminishing the nutrition of the ventricles, soon produces structural changes. Thus any particular lesion of the heart must sooner or later become a disease of the whole heart. The manifestations will, however, vary according to the origin of the lesion and the associated conditions. These manifestations do not always occur at the seat of primary disease, as is well shown in cases of mitral-valve disease, which ultimately produces death through dilatation and loss of compensation of the right side of the heart.

The conditions found in the heart are, therefore, extremely complicated and correlated, and the consideration of the pathologic physiology of the heart may be divided into:

1. The effect of cardiac lesions upon the heart itself.
2. The effect of cardiac lesions upon other viscera.
3. The effect of lesions of other viscera upon the heart.

1. The Effect of Cardiac Lesions upon the Heart Itself.—The most frequent disease of the heart is endocarditis, its lesions appearing in connection with the valves. Two chief results follow—*stenosis* and *regurgitation.* The left side of the heart is usually affected—the mitral valve most commonly, the aortic valve next. Primary disease of the right valves is rare. Taking the valvular lesions in the order of frequency, we have to consider:

A. **Mitral Insufficiency.**—This is failure of the mitral valve properly to close during the ventricular systole and prevent the blood from escaping into the auricle instead of passing into the aorta.

When the ventricular systole occurs, most of the blood passes out through the normal aortic orifice, but some returns again to the left auricle, from which it had just been received. During the auricular diastole the auricle, therefore, receives a double source of supply, blood entering from the lungs through the pulmonary veins, and from the left ventricle through the imperfectly closed auriculoventricular orifices guarded by the diseased mitral valve. This double source of supply causes the blood-pressure in the auricle to rise, so that at the time of the next auricular systole a quantity of blood beyond the normal is driven into the left ventricle, which is slightly stretched in consequence and is required to contract more forcibly to discharge the excess of blood. Hypertrophy of the left ventricle, therefore, occurs in mitral regurgitation. The hypertrophy is, however, not the result of overcoming a serious impediment to the circulation, but of successfully discharging an excessive quantity of blood.

It is, therefore, not so great as occurs in some other lesions.. The ventricle, however, as it compensates by hypertrophy for its extra labor, succeeds in driving more blood into the auricle through the insufficient valve, thus making the increased auricular pressure permanent. As the orifices of the pulmonary veins are not guarded by valves, this increase in pressure is not purely auricular, but soon increases the pressure within the pulmonary veins and their radicles, which become overdistended with blood. This may cause secondary disease of the lungs, but leaving that out of consideration at the present moment, it must be apparent that no considerable increase of pressure can occur in the distribution of the pulmonary veins without augmenting the pressure in the pulmonary artery and making it more difficult for the right ventricle to empty itself against that pressure. This increased work of the right ventricle is naturally a cause of compensatory hypertrophy which may attain considerable proportions. The balance is now quite well established, and we find that the disease of the mitral valve has resulted in hypertrophy of the left ventricle, dilatation of the left auricle, passive congestion of the lungs, and hypertrophy of the right ventricle. So long as this balance is maintained the individual is safe, but should secondary changes interfere with the integrity of the tricuspid valve,—and this can happen in hypertrophic dilatation of the right ventricle,—so that it becomes insufficient and part of the blood during the ventricular systole returns into the right auricle, not only does the right auricle become greatly embarrassed by having to work against a double obstacle,—the increased pressure in the pulmonary artery during systole and the excess of blood received during diastole,—which soon wear it out, but during the period of tricuspid insufficiency the increased blood-pressure in the right auricle, caused by the returning blood from the ventricle during systole, is felt in the venæ cavæ and a universal venous turgescence results. When the disease reaches such a stage, death is near, but its immediate cause is the embarrassment of the secondarily affected right ventricle, not of the primarily diseased left side of the heart.

The primarily diseased mitral valve, though originally incompetent, may, while the conditions above described are developing, become entirely changed through the development of fibroid changes in the diseased tissue, so that the valves not only embarrass the circulation of the blood by failing to close during ventricular systole, but also fail to open properly their contracted segment, and thus offer obstruction to the entrance of blood into the ventricle. Thus a new evil is added, which modifies the existing balance and causes further changes.

Murmurs.—The pathologic lesions are accompanied by the development of new sounds of the heart. In mitral regurgitation this sound or murmur is best heard at the apex of the organ during ventricular systole. It is variable in quality and intensity, and may consist in a long-pitched, sighing sound, or a higher pitched, blowing sound. It is synchronous with the first sound, which it may replace. Following the sound in its transmission through the chest it is most distinctly heard in the left axilla and at the angle of the left scapula. The time of the murmur is always distinctly systolic, for the reason that it is caused by the passage of the blood into the auricle during the ventricular systole.

Pulse.—The failure of the full normal quantity of blood to escape into the aorta with each cardiac pulsation naturally diminishes the acuteness of the pulse and affects its volume. The rapidity will not show marked alterations except during failure of compensation.

B. **Mitral Stenosis.**—In primary mitral stenosis the blood in the left auricle is obstructed in its passage through the auriculoventricular orifice into the left ventricle. The immediate results are that the left ventricle, failing to receive enough blood to work upon, may atrophy in uncomplicated cases. To compensate for the obstruction at the auriculoventricular orifice, the left auricle is bound to hypertrophy. The compensation thus afforded, however, increases the pulmonary pressure, impedes the exit of blood through the pulmonary capillaries, predisposes to disease of the lungs, and increases the work of the right ventricle so that the secondary cardiac involvements in mitral stenosis are practically identical with those of mitral insufficiency, and failure of compensation and death occur in the same manner.

Murmurs.—The murmur in this case is caused by the blood whirling through the constricted orifice during the auricular systole. The sound is probably formed at the mitral valve, and is most distinctly heard directly above it. The direction of the blood passing through the orifice is directly downward, so that the murmur is transmitted to the epigastrium, where it is most distinctly heard at the ensiform cartilage. It is, however, nowhere better heard than at the mitral valve itself. It can also be heard at the apex.

The time of the murmur is usually given as *presystolic*, though some writers believe it to be systolic.

Pulse.—As the essential peculiarity of the lesion is inability of the blood readily to enter the left ventricle, and from it the systemic circulation, it of necessity follows that the pulse will be small and indistinct. Combinations of mitral stenosis and insufficiency are extremely frequent, for the reason already explained.

C. **Aortic Stenosis.**—Aortic stenosis is the most frequent senile lesion of the heart. The semilunar valves, because of fibrosis or calcification, stand out in the way of the blood as it passes from the left ventricle into the aorta. In cases without complicating mitral disease the brunt of the resulting inconvenience falls upon the left ventricle, which, failing during systole successfully to discharge its contents, finds itself overdistended and obliged to work much harder. The result is compensatory hypertrophy.

Murmurs.—The murmur accompanying aortic stenosis is formed during the escape of the blood from the ventricle into the aorta. It is, therefore, systolic in time. It is most loudly heard at the point of formation—*i. e.*, over the aortic valve in the second right intercostal space.

The sound is conveyed by the blood into the vessels, and can be heard, according to its intensity, in the carotids, axillaries, and sometimes in the femorals, and even in the small arteries of the leg and foot.

Pulse.—There is nothing characteristic about the pulse of aortic stenosis.

D. **Aortic Insufficiency.**—Regurgitation of blood from the aorta into the left ventricle is extremely common in disease of the semilunar valves. The ventricle contracts, throws the blood into the aorta, but because of failure of the semilunar valves properly to close, the elastic recoil of the arterial system returns more or less of the blood into the ventricle. The left ventricle now receives, in addition to the blood passing into it from the left auricle through the auriculoventricular orifice, an almost equal quantity from the distended arteries, and distention with excessive effort and marked compensatory hypertrophy result. Some of the largest hearts result from the compensatory efforts in aortic insufficiency. As long as the mitral valve is normal, the left ventricle is alone compromised and proceeds to hypertrophy without alteration of the other chambers, increasing the length of the heart disproportionately. When the hypertrophied ventricle fails to compensate for the growing evil, or when nutritional changes supervene, the mitral orifice begins to relax, and mitral insufficiency is added, with its accompanying train of auricular distention, pulmonary congestion, hypertrophy of the right ventricle, etc.

The termination of the case is more frequently by sudden failure of the hypertrophied left ventricle to continue its labors than through the involvement of the other side of the heart. Failure of compensation is usually sudden, and sudden death is frequent in consequence.

Association of aortic stenosis and insufficiency is extremely frequent. Associated aortic and mitral disease is not uncommon.

Murmur.—The murmur of aortic regurgitation is formed at the aortic valve, and is there heard with greatest intensity. Its sound seems to be transmitted better through the sternum than other tissues, so that one can readily follow it along that bone to the xiphoid cartilage. The murmur is diastolic. Lazarus-Barlow points out that as the direction of the blood forming the murmur is toward the apex of the heart, it might be expected that it would be transmitted along the septum and best heard at the apex. The reason given for its failure to be so transmitted, which is a very plausible one, is that the murmur occurs during the diastole, at which time the apex of the heart recedes from the chest-wall.

Pulse.—The effect of the contraction of an enormously hypertrophied ventricle alternating with a sudden collapse of the arterial tension as the blood returns to the ventricle is a pulse characterized by a very forcible but suddenly collapsing quality. To it the name of "water-hammer" or "Corrigan" pulse is given. In typical cases one can readily diagnosticate the lesion of the heart by placing the finger upon the pulse.

E. **Pulmonary Stenosis.**—This lesion is usually congenital, and is commonly associated with permanence of the ductus Botalii, and frequently with imperfection of the septum ventriculorum. In rare cases it may occur in after-life because of vegetations upon the valves.

The disturbances of circulation are very complicated in the congenital cases, because of the accompanying imperfections, so that it is difficult to describe the changes. The difficulty of driving the blood through the narrowed orifice induces hypertrophy of the right ventricle.

Murmur.—There is usually a systolic murmur heard over the pulmonary area to the left of the sternum in the second intercostal space. It is like the murmur of aortic stenosis, but is not transmitted to the arterial system. The pulmonary second sound is weak and may be replaced by a diastolic murmur.

F. **Pulmonary Insufficiency.**—This also is usually dependent upon congenital malformation of the parts, the most frequent of which seems to be fusion of two segments. It may be acquired in cases of malignant endocarditis.

The condition is so rare that little positive information is at hand concerning it.

Murmurs.—The murmur is diastolic, heard over the pulmonary area, and is transmitted downward along the sternum, but, according to Osler, cannot always be differentiated from the murmur of aortic insufficiency.

G. **Tricuspid Stenosis.**—This lesion may be congenital or acquired. It is uncommon, and in the majority of cases is secondary to disease of the left side of the heart, and forms one of the most serious complications of mitral stenosis. The inability of the blood to pass the tricuspid orifice causes engorgement of the venæ cavæ. Cyanosis and dropsy are the chief symptoms.

Murmur.—A presystolic murmur can usually be heard in the midsternum near the ensiform cartilage. The murmur does not appear to be transmitted.

H. **Tricuspid Insufficiency.**—This is a frequent affection, occurring after endocarditis, though more frequently after diseases of the lungs associated with obstruction of the circulation. It thus accompanies emphysema, chronic bronchitis, and fibroid induration. The circulation becomes embarrassed by the return of blood into the right auricle, retention of blood in the venæ cavæ, consequent cyanosis and venous engorgement, such as characterize tricuspid stenosis and mitral regurgitation.

Murmur.—There is a murmur, systolic in time, but heard at the midsternal line and transmitted toward the epigastrium. The murmur is usually soft and low, by which it can be differentiated in a few cases from the higher pitched and harsher mitral murmurs. It may rarely be heard as far as the axilla, but usually is limited in distribution.

TABLE OF ENDOCARDIAL MURMURS.[1]

ORDER OF FREQUENCY.	AREA.	TIME.	TRANSMISSION.	LESION.
1. Mitral regurgitation . . .	Apex.	Systolic.	Left axilla and angle of left scapula.	Insufficiency.
2. Aortic obstruction . . .	Aortic.	Systolic.	Into carotid.	Stenosis or roughening.
3. Aortic regurgitation . .	Aortic.	Diastolic.	Along sternum to ensiform.	Insufficiency.
4. Mitral obstruction . . .	An inch above apex.	Presystolic.	Not transmitted.	Stenosis.
5. Tricuspid regurgitation .	Midsternal.	Systolic.	Toward epigastrium.	Insufficiency.
6. Tricuspid obstruction . .	Midsternal.	Presystolic.	Not transmitted.	Stenosis.
7. Pulmonary obstruction .	Pulmonary.	Systolic.	Into pulmonary.	Stenosis or roughening.
8. Pulmonary regurgitation	Pulmonary.	Diastolic.	Downward along sternum.	Insufficiency.

The Formation of Cardiac Murmurs.—The murmurs of valvular defects were supposed by Lænnec to depend upon the resistance which the blood meets in passing through the roughened and narrowed valvular orifices. Recently, however, a different theory has received strong support, and it is now commonly believed that the sound depends upon the eddies that are formed by the circulating blood as it passes rapidly through a narrow opening into a larger space. The arguments in favor of this theory are that murmurs are sometimes heard when no valvular defects exist, and that under certain circumstances murmurs develop in the veins outside of the heart, without any roughening to account for them. It is also true that valvular defects sometimes exist without murmurs, and that the loudness and quality of the murmur bear no relationship to the character of the valvular lesion.

The blood-pressure makes great difference in the character of a murmur, increase of pressure being associated with increase in its harshness, diminution of the pressure with diminished harshness and sometimes with its disappearance. For this reason the examination of the heart of a patient quietly reclining in bed or in an easy-chair should not be sufficient, but some muscular efforts should be required by which his blood-pressure will be elevated and any existing murmur made audible.

Cardiac failure is the inability of the heart to maintain its functional activity.

1. EXTRINSIC CAUSES.—*Anemia* (pernicious anemia), *infection*, and *intoxication* may bring about degenerative changes in the heart muscle, which destroy its contractile powers. In pernicious anemia the very marked fatty degeneration is sufficient to account for the failure, and in typhoid fever and other infectious and toxic processes the hyaline and fatty changes, as well as the occasional fragmentation of the cardiac muscles, explain it.

Violent Muscular Activity.—Extreme muscular activity produces a very marked increase in the blood-pressure, and throws a marked strain upon the left ventricle. This, with its involved changes, is experienced by all who make occasional, though unusual, efforts,—running for a car, hastening up a long flight of stairs, riding a bicycle up-hill, etc.,—and manifests itself in shortness of breath and palpitation which become decidedly uncomfortable. Carried to an extreme degree, this increase of pressure and sudden unwonted action of the heart may bring about its acute dilatation and ultimate failure.

Rupture of the heart or of aneurysms, with escape of blood into the pericardium, may cause death in a few moments by pressure upon the auricles and great veins and preventing the entrance of blood into the heart, thus lessening the output of blood from the ventricles and leading to death from obstruction of the circulation.

Asphyxia.—Whether caused suddenly by ligation of the windpipe, or slowly by disease of the lungs, cardiac failure is the invariable outcome.

With the cessation of oxygenation and the accumulation of CO_2 in the blood, the medulla oblongata is stimulated and sends inhibitory impulses to the heart along the pneumogastric nerve. The tendency of these impulses is to slow the heart and diminish the discharge of blood from the ventricles. The stimulation of the respiratory center now causes active muscular movements whose tendency is to increase the blood-pressure in the great veins and increase the quantity of blood that is to enter the heart, thus tending to increase the work of the right ventricle in spite of the inhibitory influences.

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[1] Tabulated by Dr. B. Franklin Stahl.

Increasingly powerful impulses reach the heart through the cardiac nerves, tending to overthrow the effect of the pneumogastric stimulation and increase the ventricular action and produce rise of blood-pressure in the aorta.

The condition is well described by Lazarus-Barlow : " Four forces are acting upon the right heart: (1) Upon the ventricular wall are acting (indirectly) accelerator impulses which call for contraction of the ventricle at whatever cost, on behalf of the body generally, and besides them—(2) inhibitory impulses which, though protecting the heart, nevertheless, at the same time, lead to diastolic dilatation of the ventricle ; (3) behind is an enormously increased venous pressure ; (4) in front is an impediment in the shape of increased aortic pressure. But from the nature of the case the initial difficulty—*i. e.*, the deficient aëration of the blood—not only continues, but becomes rapidly more urgent, and ultimately the cardio-inhibitory center becomes itself asphyxiated and ceases to act, and the heart, left in a dilated condition and having itself been supplied during the crisis with venous blood, is given over to the unrestrained action of the three remaining forces. Unrestrained by vagus action, and perhaps directly urged by the accelerators, overfilled during diastole, it contracts rapidly but feebly, until at last the dilatation is such and the exhaustion is such that it can no longer cope with its contents. Even the whole reserve power of the ventricle is not, as a rule, used up, for if an incision be made into the arrested right ventricle of a dog that has been asphyxiated, there will be a short return of systolic contraction when a portion of the imprisoned blood has escaped through the artificial opening."

2. INTRINSIC CAUSES.—The intrinsic causes depend upon pericardial adhesions, valvular defects, thrombi, congenital defects, and other conditions which necessitate a very marked increase in the work of the heart. It is true that all these causes are of more or less protracted duration and associated with the condition of hypertrophy known as *compensation*, but as the defects to be compensated for are not in most cases constant in quality, but increase in the course of time,—stenosis following insufficiency of the valves, growth of thrombi, neoplasms, etc.,—the hypertrophy required to maintain the equilibrium is increasing and the demands upon the muscular wall more and more exacting, until the excess of labor is followed by exhaustion and the hypertrophied ventricle fails to respond, dilates, and "compensation has failed."

In addition to these conditions it must be remembered that the conditions that occasion valvular defects also occasion arterial defects, and that the coronary arteries, being situated at a short distance from the aortic valves, are early diseased, thus obstructing the normal supply of blood to the ventricular walls and hastening the retrogressive changes.

Indeed, disease of the coronary arteries may cause death in hearts free of valvular defects and without hypertrophy—*angina pectoris*—just as well, though not so frequently, as in hypertrophied hearts with valvular defects.

In nearly all cases of failure of compensation failure of nutrition plays an important part.

II. **The Effect of Diseases of Other Viscera upon the Heart.**—While it is unquestionably true that the heart is profoundly influenced in exophthalmic goiter (*q. v.*), for some reason not yet positively determined, and equally influenced in certain psychic conditions, as well as more or less disturbed in dyspeptic affections, the organs whose morbid conditions most profoundly influence the heart are the lung and the kidney.

A. **Effect of Pulmonary Disease upon the Heart.**—The pulmonary diseases that exert the most marked influence upon the heart are characterized by obstruction of the vessels and embarrassment of the right heart. The chief of these is *emphysema* (*q. v.*), in which the walls of the air-cells are unduly stretched, the capillaries also stretched and attenuated, and finally obliterated. The work of forcing the blood through the narrowed capillaries, and the greater work of getting all the blood through the diminished number of capillaries, falls upon the right heart, whose ventricle compensatorily hypertrophies. The patient experiences little difficulty so long as the hypertrophy is sufficient, but as the pulmonary conditions become worse and worse, the tax upon the ventricular wall increases and dilatation with tricuspid regurgitation come on. With the tricuspid regurgitation appears most marked venous engorgement, as the blood which should be passed out of the pulmonary artery is in part returned to the right auricle and retards the escape of blood from the veins.

In this manner pulmonary obstruction reacts upon the heart and may cause death by failure of the right ventricle successfully to compensate.

B. **Effect of Renal Disease upon the Heart.**—Nephritis reacts upon the heart through poisons which are retained in the circulation and stimulate the vasomotor nerves. Through their action the arterial blood-pressure is increased and extra labor thrown upon the left ventricle, which hypertrophies. The hypertrophy is rarely great.

III. **The Effect of Disease of the Heart upon the Other Viscera.**—Every departure from the normal action of so important an organ as the heart is attended by disturbances in some part of the economy. The most marked general effects are shown in chronic heart disease, where the venous congestions are characterized by cyanosis, congestion of the lungs, general venous congestion, with consequent cirrhosis of the liver and kidneys, varicose veins, hemorrhoids, ascites, edema, general tissue malnutrition, and general predisposition to infection of all kinds.

DISEASES OF THE ARTERIES.

Hypertrophy of the arteries is not uncommon, and is seen in cases in which permanent collateral circulation is established and in all cases in which hypertrophic or neoplastic formations cause any part of the body to require a constantly increasing blood-supply.

Atrophy of the arteries, depending upon profound anemia and marasmus, may be general to the entire vascular system, and may occur simultaneously with atrophy of the heart from the same general causes.

Local atrophy of arteries is seen to follow obstruction by ligation, thrombosis, etc. The artery no longer being required for the transmission of blood, gradually diminishes to a mere fibrous cord, the muscular tissue all disappearing. In cases of amputation the arteries of the stump diminish in size in keeping with the needs of the tissues to be supported.

Atrophy of the muscular tissue occasionally follows overdistention of the vessels.

Fatty degeneration of the arteries may affect the intima, the media, or the adventitia.

Fatty degeneration of the intima occurs in the larger vessels and in the capillaries. In the former it is most common in the condition later to be described as *atheroma*, and depends upon disturbances of circulation in the vasa vasorum. In the latter it is the result of profound anemia, marasmus, and certain forms of intoxication. Profound hemorrhages are also sometimes followed by sudden fatty degeneration of the capillary blood vessels of the retina, with hemorrhage and consequent sudden blindness.

In the larger vessels the lesions appear as larger or smaller, opaque, yellowish-white, slightly elevated spots. When a section is made through such a spot, the endothelial cells are found infiltrated with fatty granules and are sometimes desquamated. The lower layers of the intima contain occasional areas filled with fatty droplets.

Fatty degeneration of the media affects the muscle-cells, which are gradually destroyed. By diminishing the resisting power of the vessel-wall, the condition predisposes to rupture of the vessel or yielding of its wall, with the formation of aneurysm. Calcification of the media very frequently follows the fatty change, probably depending upon the same cause.

Fatty degeneration of the adventitia is without much interest or importance. It occurs in inflammatory conditions and in various necroses, etc.

Amyloid disease of the arteries is common, especially in the smaller vessels of the liver, kidney, and spleen. The change is first seen in the intima of the larger vessels and the media and adventitia of the smaller ones. The change can be observed to excellent advantage in the delicate capillary loops of the renal glomeruli.

Hyaline degeneration of the vessels is not uncommon. Unfortunately, the latitude given by authors to the term "hyaline" makes it probable that not all the conditions in which it is said to occur are similar. Probably the most frequent occurrence of hyaline degeneration takes place in the intima of the large arteries and results in its gradual transformation into homogeneous, anuclear substance descending to the media and involving some of the muscle-cells. This change often marks the inception of atheroma.

Calcification of the vessels is common in old age and in chronic inflammatory conditions. It depends largely upon an altered or diminished circulation within the vasa vasorum. Calcification of the intima of the vessel following atheromatous changes takes the form of calcareous plates, which may be deposited beneath the endothelial layer or may project through it and appear like fish-scales imbedded in the tissue.

In senility it is most frequent in the media, where the mineral salt is deposited in streaks between the layers of muscular tissue. Sometimes the deposit takes on an annular form, and it may reach so extreme a degree that the vessel is transformed into a brittle, calcareous pipe—the "pipe-stem artery." In the aorta and large vessels the calcareous salts are sometimes deposited between the elastic lamella. The deposit of mineral salts rarely takes place in the capillaries except in a few tumors of the central nervous system.

The lime-salts are usually deposited in the vessel-wall in the form of fine granules, which later unite to form plates or lamina. Rarely true bone is formed in the vessel-wall.

Necrosis and **gangrene** of the blood-vessels are unusual, but occur in gangrene of the limbs and in severe and destructive inflammatory conditions with gradual extension to the vessel-wall and when gangrene occurs in the immediate vicinity. Necrosis with erosion of the arteries is not uncommon in pulmonary tuberculosis with excavation, and may lead to diminution of vascular resistance, with fatal hemorrhage from rupture.

ARTERITIS.

Inflammations of the arteries may originate within or without the vessel: very rarely from the vessel-walls themselves, in consequence of micro-organisms deposited in them by the vasa vasorum.

Endarteritis, corresponding to endocarditis, is an inflammation resulting from mechanical or chemical irritation. Such irritants are usually emboli resulting from endocardial vegetations, destroyed valves, softened thrombi, etc. The irritation immediately exerted upon the intima causes it to become roughened and clouded and to lose its endothelium. Not infrequently it becomes infiltrated with round-cells. The vasa vasorum are enlarged, and the vessel itself is swollen and hyperemic. The condition is succeeded by the formation of a thrombus in the lumen of the vessel.

Periarteritis is a vascular inflammation that follows the extension of inflammatory conditions in tissues contiguous to the vessel-wall, or from approximated foci of suppuration or gangrene. The disease begins outside and slowly invades the coats of the vessel. The adventitia appears injected, edematous, and swollen, and is slowly loosened in texture by the purulent infiltration of its tissue. The subjacent coat is gradually invaded, and if the disease progresses, the intima may be reached. The vessel becomes inelastic, the swelling contracts the lumen, and retrogressive changes may occur in the muscular substance. If the inflammation extends to the intima, its surface becomes roughened, the cells detach, and thrombosis is almost sure to follow. The lodgment of infectious emboli brought by the vasa vasorum may cause abscess formation in the walls of the larger vessels. Such abscesses evacuate into the blood-stream.

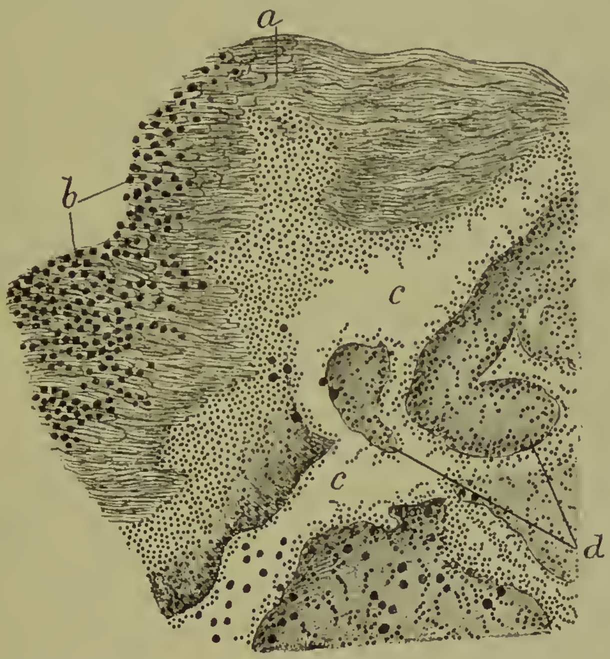

FIG. 239.—Acute arteritis resulting from streptococcus infection: *a*, Necrotic and eroded intima; *b*, small round-cell infiltration of the intima; *c*, spaces and cracks in the necrotic intimal tissue; *d*, detached fragments of the necrotic tissue. The streptococci are invading the tissue in all directions (Weichselbaum).

Sclerotic arteritis, chronic arteritis, arteriosclerosis, or arterio-capillary fibrosis, is one of the most frequent and most important diseases of the blood vessels. It may be defined as a fibrous induration of the arterial walls, associated with nutritional and degenerative changes. It is the premature or excessive occurrence of changes inevitable to old age.

Etiology.—The causes of arteriosclerosis are numerous and varied, and produce the characteristic changes in different ways.

Heredity seems to have a distinct influence upon its occurrence.

Race may have some influence. Negroes are said to show the disease more frequently and earlier than Caucasians. The disease is almost entirely confined to human beings, being almost never observed in the lower animals.

Senility is almost invariably associated with vascular sclerosis. It may, however, occur in early life. I have seen a moderately well-marked aortic sclerosis with atheroma in a little girl (negress) only twelve years of age. As a rule, the disease is more frequent beyond middle life, and increases in frequency with added years. Sometimes very aged persons show no signs of it.

Sex seems to play a distinct part in the development of arteriosclerosis, the disease being more frequent in men than in women, because of their occupations and habits.

Occupations.—Exertion is a very important etiologic factor, because of the unequal blood-pressure that it occasions. When from any cause the arteries are predisposed to sclerosis, the occasional extreme variations of blood-pressure produced by overexertion become of great importance as exciting causes of further changes.

Hypertrophy of the heart, by increasing the vascular tension, acts in the same manner as overexertion.

Intoxication.—Alcoholism is thought to be one of the most important causes of arteriosclerosis. *Lead* is another important cause. *Gout* is almost invariably associated with arteriosclerosis, and probably is one of its most important causes. Other intoxications by leukomains, indol, etc., are probably of importance.

Disease of the kidneys predisposes to diseases of the arteries both by systemic intoxication and increased blood-pressure.

Infection.—Rheumatism is probably the most important infection leading to arteriosclerosis. *Syphilis* is the cause of numerous lesions of the blood vessels, arteriosclerosis being a common one.

Tuberculous arteriosclerosis is comparatively unimportant. Its lesions are always local and circumscribed, and are more apt to be necrotic than sclerotic.

The operation and coöperation of the various etiologic factors will be clear from the following description of its morbid anatomy:

Morbid Anatomy.—The sequence of events in arteriosclerosis depends upon the etiology of the particular case. Some look upon the changes in the media of the vessels, some upon the changes in the blood-pressure, some upon direct damage of the vessel-walls by circulating poisons, and some upon disease of the vasa vasorum as the primary starting-point of the disease.

The disease is most common in the *large vessels*, especially the *aorta*. With advancing age there is a universal tendency for the entire arterial system to undergo a certain amount of fibroid change. It is easy to understand that the increase of connective tissue in the walls of the vessels, accompanied as it is by the disappearance of some of the muscular tissue, and often by changes in the elastic lamina constituting the fenestrated membrane, causes them to become rigid, and, in consequence, less distensible than normal. If with this change of the vessels the heart be overstimulated by exertion, etc., the increased blood-pressure, exerting its distending force upon the vessel-wall, can easily cause insignificant cracks of the media, followed by more or less reactive inflammation, with round-cell infiltration, and more connective-tissue proliferation. The vas vasorum that happens to be embraced in the fibroid area become compressed and perhaps occluded, and the nutrition of local areas of the vessel-wall is cut off, to be followed by retrogressive changes—softening and hyaline and fatty degeneration.

The connective-tissue proliferation forms the *sclerosis*, while to the nutritive changes following or associated with it the term *atheroma* is applied. It is thus seen that arteriosclerosis is a composite process which begins as a retrogressive tissue change, transforms itself into secondary inflammation with reparative cicatricial scleroses, and causes a tertiary nutritive disturbance—atheroma.

Arteriosclerosis may be a local circumscribed lesion,—*arteriosclerosis circumscripta* or *nodosa*,—or may be so widely distributed in large vessels and especially in the aorta that it may be difficult to find any normal tissue—*arteriosclerosis diffusa*.

1. In the *circumscribed form of arteriosclerosis* one finds, here and there upon the inner surface of the vessel, rounded, oval, stellate, irregular, or linear elevations of a yellowish-white or whitish color and consistence, varying with their structure. If it consists of connective tissue, the lesion may be firm and almost cartilaginous. If, on the other hand, it has undergone retrogressive degeneration, which is common, it may be friable or mucilaginous.

The surface of the larger rounded patches or plaques is sometimes smooth, sometimes dimpled, sometimes roughened. The softened, atheromatous plaques are formed through degeneration of local areas of the intima, from which the blood-supply has been shut off. Their covering consists partly of degenerated endothelium with a few connective-tissue fibers easily torn with the finger-nail. When lacerated, a softened, pap-like mass, which has resulted from the combined fatty and hyaline degeneration of the tissues of the intima and subjacent media, escapes.

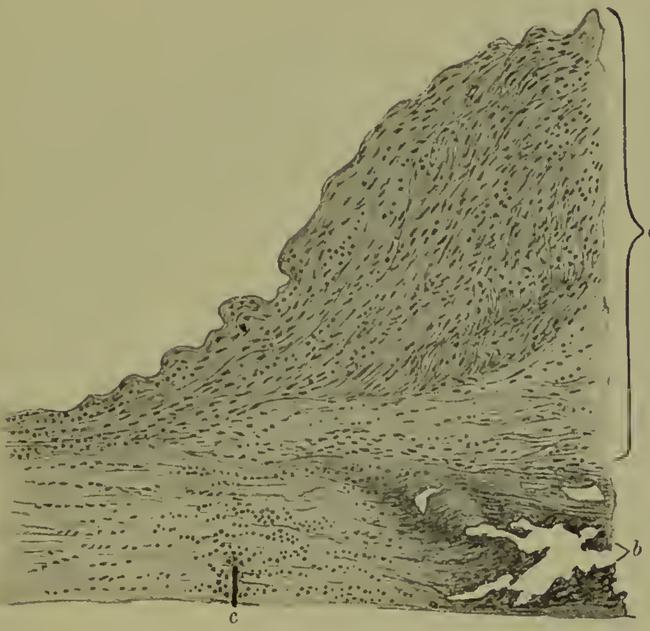

FIG. 240.—Atheroma of the aorta: *a*, Thickened intima; *b*, calcareous deposit in the media; *c*, cellular infiltration of the media (Weichselbaum).

The small cavity is spoken of as an *atheromatous cyst*. The word "atheroma" comes from the Greek, *ἀθήρη*, mush or pap, and *ὄμα*, tumor. At one time it was thought from its appearance that the matter contained in these cysts was pus, but if it be examined microscopically, it is found to consist of fatty granules, with margarin and cholesterin crystals. When the atheromatous cysts have persisted for some time, lime-salts are commonly deposited in the granular débris in the form of fine particles. These later coalesce and form a calcareous mass or plate the size and shape of the cavity in which they form. In the course of time the badly nourished endothelial covering is lost by degeneration and exfoliation, and the edges or surfaces project upon the inner wall of the vessel. The degeneration of the intima may advance too quickly to permit of calcification, and may even extend through its entire thickness, causing the formation of excavated defects known as *atheromatous ulcers.*

The atheromatous ulcer causes the vascular wall to become thin and abnormally yielding, to compensate for which nature proceeds to back it up with an additional connective-tissue support, thus increasing the fibroid changes, diminishing the distensibility, and predisposing to further cracks and more cicatricial and atheromatous changes until the entire vessel—especially the aorta—may become diseased. This progressively increasing fibrosis and elasticity are followed by hypertrophy of the left ventricle, with resulting increase of the blood-pressure and consequent exaggeration of the whole process. The cicatrization of the atheromatous ulcers is slow. Yielding of the vessel-wall with cylindric, fusiform, or saccular dilatations (aneurysms) is frequent in consequence of the loss of elasticity, and the deposition of fibrin upon the roughened surfaces is very common. The atheromatous lesion is also a not infrequent point of entrance for infectious organisms which accelerate the destructive lesions.

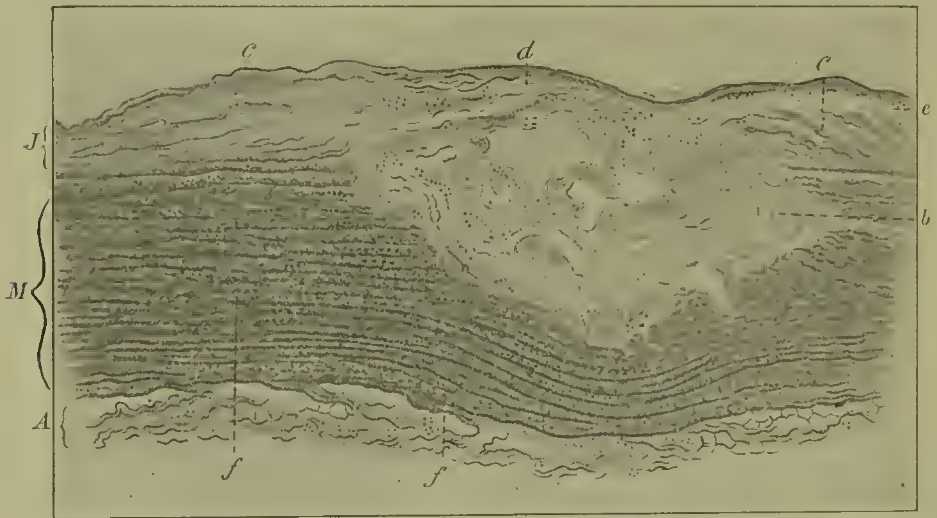

FIG. 241.—An atheromatous patch in the abdominal aorta which has not yet broken through: *J*, Intima; *M*, media; *A*, adventitia; *b*, atheromatous necrotic focus in the intima and media; *c*, elastic fibers of the intima; *d*, elastic fibers which have persisted between the necrotic focus and the endothelial layer; *e*, thickened endothelium; *f*, infiltration of the media with small cells (Dmitrijeff).

In the *smaller vessels* of the brain, etc., rupture with hemorrhage (apoplexy) is a common consequence of sclerotic endarteritis and atheroma. Such hemorrhages may be fatal.

In the smaller vessels one of the most important effects of the disease is the diminution of the lumen (endarteritis deformans), with insufficient nourishment of the tissue in its distribution, by which various necrotic and ulcerative lesions can be produced. Not infrequently the diseased vessel, already nearly closed, is permanently obliterated by thrombosis and its subsequent changes (endarteritis obliterans) and may lead to gangrene.

Thoma is of the opinion that the diffuse arteriosclerotic process, which he calls primary, occurs in consequence of stretching from increased blood-pressure, and views the process as essentially reparative (compensatory) in nature. The not uncommon lesions of the arch of the aorta in which the sclerotic change occurs chiefly in the form of somewhat parallel lines, and which have, from their resemblance to the drooping branches of a weeping-willow tree, been termed the "willow markings," may serve as examples of the effect of blood-pressure in injuriously distending the aorta.

Those who look upon the process as originating in embolic, thrombotic, or sclerotic changes in the vasa vasorum must find it difficult to account for cases in which the atheroma is limited and the sclerosis wide-spread and marked.

When the disease follows lead or alcohol intoxication, it may begin in the vasa vasorum and lead to a gradual perivascular inflammation with connective-tissue proliferation, obstruction, atheroma, reinforcement by connective-tissue, further disturbance in the nutritive vessels, and greater resulting atheroma and sclerosis.

The exact rôle of infection in arteriosclerosis is not clear. It follows rheumatism, endocarditis, typhoid fever, scarlatina, syphilis, etc., but may, in these cases, have something to do with mycotic embolism of the vasa vasorum. It may also have something to do with the general circulatory disturbance, or it may be that a slight existing disease is accelerated and exaggerated by the infection, just as an old sclerotic endocarditis may become malignant through an attack of an infectious disease.

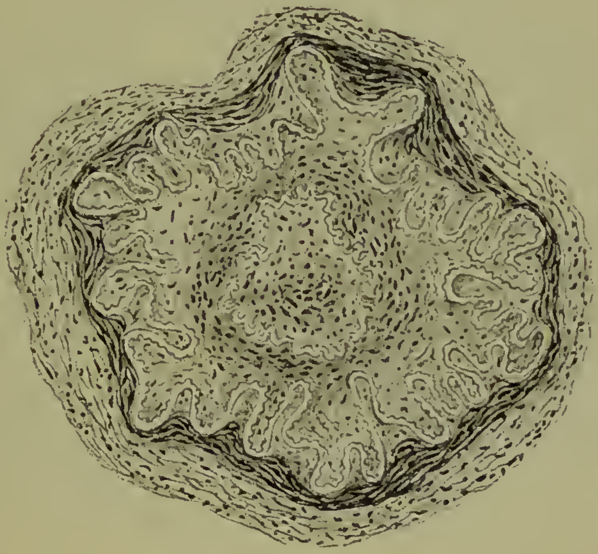

FIG. 242.—Endarteritis productiva (Dürck).

The aorta is the most frequent seat of sclerotic arteritis. It is usually most marked in the ascending aorta, next in the arch, and least so in the descending aorta. It is commonly associated with disease of the aortic valves, and is very apt to embrace the coronary arteries, especially at their origin. The splenic artery, the arteries of the brain (especially the vertebrals and basilar), and the arteries of the uterus are commonly affected. Any artery of the body may be the seat of the disease.

The affected aorta is apt to be dilated—sometimes enormously so. Its walls may appear smooth, but usually the intima is ridged, seamed, nodular, and calcified. It is mottled in color from alternating normal tissue, yellow-white or whitish atheromatous patches, glistening, calcareous plates, ragged, reddish ulcers, and patches of red fibrin precipitated upon it. The finger, upon passing over the surface, may receive a gritty sensation if mineral matter is present.

The changes may be limited in the intima, consisting of the atheromatous ulcers, cysts, nodes, and calcified areas, or may involve the media to a considerable degree.

The connective-tissue proliferation occurs chiefly in the lower layers of the intima, but also in the media and in the adventitia. The elastic and muscular tissues may atrophy. Round-cell infiltrations occur about the nutrient vessels. Immediately beneath and around the atheromatous ulcers round-cell infiltrations with beginning reparative hyperplasia of connective tissue are observed.

2. *The diffuse form of arteriosclerosis* is commonly spoken of as *arteriocapillary fibrosis.* Its chief effects are upon the smaller arteries and capillaries, which undergo thickening of the walls, with reduction of caliber, and may be completely obstructed (endarteritis productiva; endarteritis obliterans). The changes affect the vessels quite uniformly, and are chiefly situated in the intima and media, which undergo hyaline degeneration. In many places the elastic-tissue lamina may entirely disappear. The obstruction of the vessels is associated with atrophy of the parenchyma of the organ, to which the vessel distributes. The most typical lesions are probably observed in the kidney (see Arteriosclerosis of the Kidney). The diffuse form of arteriosclerosis is common in nephritis and in hypertrophy of the heart. The arteriocapillary fibrosis is probably one of the important predisposing causes of the nodular form of the disease.

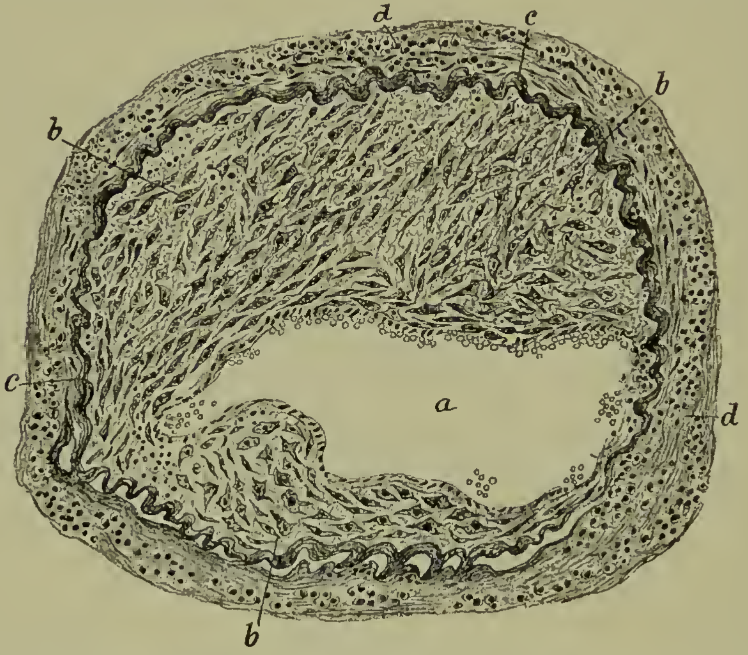

FIG. 243.—Syphilitic arteritis: *a*, Greatly diminished lumen of the vessel obstructed by the eccentric growth of embryonal connective tissue of the intima *b*; *c*, fenestrated membrane; *d*, media infiltrated with round-cells (Weichselbaum).

When the sclerotic changes in the aorta are quite diffuse and associated with disappearance of much of the muscular tissue of the media, a very marked dilatation commonly occurs. In such cases the aorta appears enormously capacious, and may have numerous shallow pouchings at its thinner points.

The aortic dilatation bears a slight resemblance to ectatic aneurysm, but is not sufficiently circumscribed or exaggerated to be so classified.

The aortic orifice of the heart is usually much relaxed and larger than normal, and the valves are large and flaccid. Hypertrophy of the heart is usually present in such cases.

Syphilitic Arteritis.—In the local lesions of syphilis the included blood vessels undergo inflammatory changes not essentially different from those seen in other subacute inflammatory conditions and not infrequently terminating in *endarteritis obliterans*. In addition to these, however, there are in both the local lesions of early syphilis and in chronic tertiary syphilis certain changes of the blood vessels which are well marked, though not sufficiently characteristic to establish a microscopic diagnosis of the disease.

In both local and general syphilis the arterial lesions consist chiefly in a cellular proliferation. In the neighborhood of local lesions it begins in the adventitia and proceeds inward, causing each coat of the artery, but especially the intima, to become markedly thickened through proliferation of the connective tissue. The encroachment upon the lumen may amount almost to obliteration.

The infiltrating cells are partly round-cells, partly fibroblasts. In tertiary syphilis, the cellular infiltration and proliferation may take the form of more or less circumscribed collections of round- and spindle-cells, with giant-cells exactly corresponding to those seen in tuberculosis. This lesion, no doubt, corresponds to miliary gumma (arteritis gummosa).

The syphilitic lesions are distinguishable from those of sclerotic arteritis in that their cellular proliferations show little disposition either to degenerate or advance to the formation of perfect connective tissue. Atheroma also begins in the intima, while Schmaus insists that the syphilitic affections of the vessels begin in the adventitia.

The vessels most commonly affected in syphilis are those of the base of the brain. The elasticity of the vessels is much compromised by the disease, and at times ruptures; at others aneurysmal dilatations may be observed as sequelæ.

Tuberculous arteritis occurs by direct extension to blood vessels by continuity and contiguity of the tuberculous tissue. It also occasionally occurs primarily in cases in which tubercle bacilli entering the vasa vasorum are deposited in the wall of the vessel and lead to local primary tubercle formation. In the former case the adventitia is first affected; in the latter, the media or intima. In the smaller vessels the result is invariably endarteritis obliterans, but in large vessels, like the aorta, the lesion becomes covered with a fibrinous deposit and continues slowly to spread.

Fortunately, tuberculous aortitis is very rare, and the tissues of the aorta are very resistant, so that the disease may continue for a long time without necessarily causing either rupture or aneurysm. It may lead to miliary tuberculosis.

In the smaller vessels, which are so commonly affected in pulmonary tuberculosis, aneurysmal dilatation in consequence of weakening of the vessel-wall from caseous tubercles is very common, and rupture, with hemorrhage of varying size,—not infrequently fatal,—is one of the frequent accidents of pulmonary phthisis.

Periarteritis nodosa is a peculiar affection of the small arteries characterized by the occurrence of small fibrous thickenings of the adventitia. These are quite circumscribed, and seem sometimes to be of inflammatory origin, sometimes to be small aneurysms containing organized thrombi. In some cases they may be, as Eppinger has suggested, imperfections of development. They may also at times result from infection. They are most common in the arteries of the muscles and serous membranes, spleen, abdominal and pelvic organs, and uterus. Many of the little nodes may be present upon a single artery.

ANEURYSM.

An aneurysm is a circumscribed dilatation of an artery, resulting from the effect of the blood-pressure upon an injured or diseased vessel-wall.

Etiology.—There are two determining causes of aneurysm: 1. Injury or disease of the vessel-walls. 2. Arterial blood-pressure.

1. **Injury and Disease of the Vessel-walls.**—*Traumatism* sometimes

plays an important part in the etiology of aneurysm, but *disease of the vessel-walls* is by far the most frequent cause. Of the vascular diseases, the most common and most important is *arteriosclerosis*. As arteriosclerosis follows a number of constitutional maladies, it is commonly said that age, alcoholism, overexertion, syphilis, gout, plumbism, etc., are predisposing causes of aneurysm. They predispose to it, however, solely by bringing about such arteriosclerotic changes as may permit the yielding of the arterial walls. As arteriosclerosis most frequently affects the aorta and great vessels, so aneurysm is most frequent in those vessels. It occurs just at the age at which arteriosclerosis develops. Of 92 cases studied by Hayden, 60 occurred between the thirtieth and sixtieth years.

Syphilis and *tuberculosis* may produce aneurysm by directly affecting the tissue of the vessel-wall and causing a destructive periarteritis. The best illustration of this is seen in the walls of tuberculous cavities of the lung, where aneurysmal dilatations of the vessels are not infrequently observed in consequence.

Thrombosis sometimes causes aneurysm through the reactive changes in the vessel-walls and the increased pressure in the vessel above the obstruction.

Parasitic disease of the vessels, such as is produced in the mesenteric arteries of horses by the worm known as Strongylus armatus, and by the occasional invasion of the vessel-walls by bacteria, may predispose to aneurysmal dilatation.

2. **Arterial Blood-pressure.**—It is the persistent distending force of the blood-pressure that finally effects the yielding of the weakened vessel. If the vessel is very weak, it may rupture, but if its resistance is lessened to a degree not permitting of rupture of all the coats, rupture of some of them, with persistence of the others, or a gradual yielding of all the coats, may take place. The greater the blood-pressure, the greater the liability to aneurysm. The pressure may act slowly for a long time to effect the dilatation in cases in which all the walls are involved, or a sudden great increase of the pressure may abruptly rupture some of the arterial coats and cause an aneurysm of rapid formation.

Morbid Anatomy.—Aneurysms may be single or multiple. They may be of enormous size, or may be scarcely visible to the naked eye, as the miliary aneurysms of the cerebral vessels.

The most frequent seats of aneurysm are the aorta, popliteal, femoral, subclavian, carotid, axillary, innominate, external iliac, common iliac, posterior tibial, gluteal, internal iliac, temporal, vertebral, subscapular, brachial, and radial arteries. According to Crisp' s statistics of aneurysms of the peripheral vessels, their relative frequency is as follows:

Popliteal	187	Posterior tibial	4
Femoral	78	Gluteal	2
Subclavian	35	Internal iliac	1
Carotid	34	Temporal	1
Axillary	26	Vertebral	1
Innominate	23	Subscapular	1
External iliac	16	Brachial	1
Common iliac	4	Radial	1

The most frequent seat of aneurysm is the aorta. Of 915 cases of saccular aneurysm collected by Crisp, 328, or 41 per cent., affected the arch of the aorta; 105, or 11 per cent., the abdominal aorta, the remainder occurring in other vessels.

Of 109 cases of aneurysm which occurred in the British army, 37 arose from the ascending arch, 38 from the arch itself, 12 from the descending arch, 7 in the thoracic, and 15 in the abdominal aorta.

Of 101 cases studied by Malmsten, 57 arose from the arch, 17 from the descending, and 4 from the abdominal aorta.

Of 234 aortic aneurysms studied by Crisp, 175, or 74.8 per cent., arose from the thoracic aorta, and 59, or 25.2 per cent., from the abdominal aorta and its branches. Of 167 aneurysms of the thoracic aorta, he found 98, or 58.8 per cent., arising from the ascending part, and 48, or 28.7 per cent., from the arch itself, while 21, or 12.6 per cent., arose from the descending aorta.

I. True aneurysms are formed by dilatation of all the arterial coats.

II. False aneurysms, by dilatation with rupture of some of the arterial coats.

According to their morphology, aneurysms are divided into—

1. *Ectatic Aneurysms.*—These are true aneurysms, and consist of cylindric or fusiform dilatations embracing a considerable length of an artery. A dilated vessel that becomes spirally twisted is known as a *cirsoid aneurysm.* This condition is not infrequently found in the splenic artery.

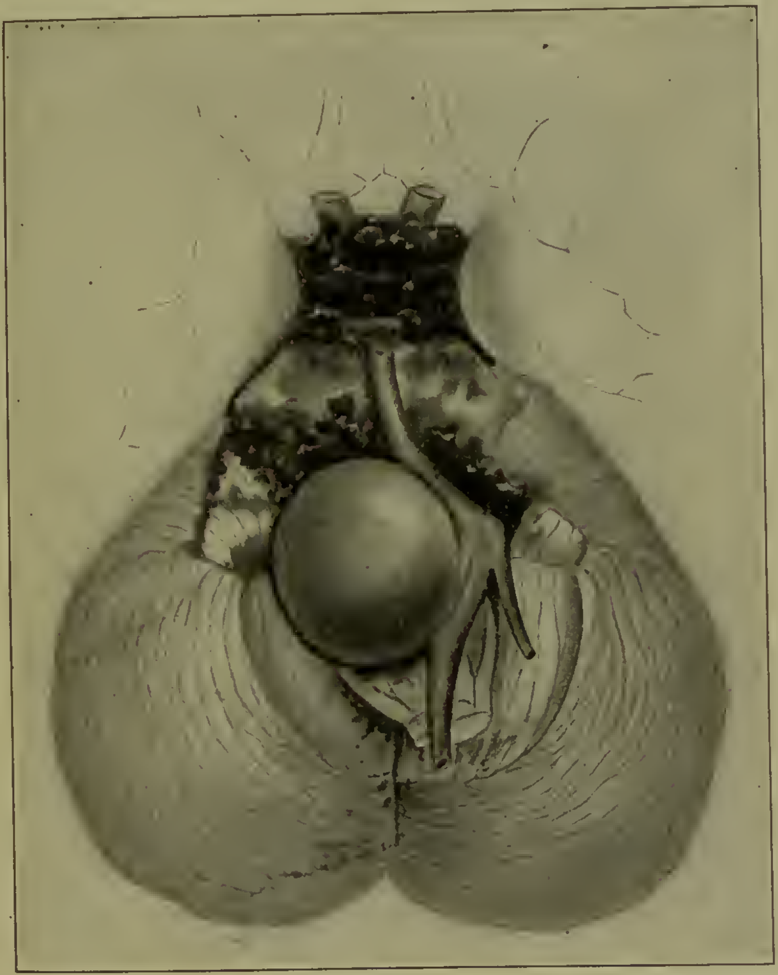

FIG. 244.—Saccular aneurysm of the vertebral and basilar arteries (Bollinger).

Ectatic aneurysms may eventually become dissecting aneurysms should the walls rupture.

2. *Saccular aneurysms* form in consequence of local lesions of the arterial wall, the dilatation resulting in the formation of a pocket or diverticulum. They may be true aneurysms, but are frequently false aneurysms with imperfect walls.

3. *Dissecting aneurysms* occur in consequence of partial rupture of an arterial wall. The blood slowly escaping dissects the intima from the media, or the media from the adventitia, thus forming the aneurysmal sac. Such

aneurysms are usually irregular in form, sometimes saccular, but more often working along the length of the vessel for a considerable distance. The walls of a dissecting aneurysm are usually somewhat reinforced by newly formed connective tissue on the outside, and by deposits of fibrin on the inside.

Aneurysms, for the most part, feel like solid tumors, not like empty sacs, their firmness depending upon contained thrombi.

Seen from within, the aneurysm appears like a tumor composed of an irregular mass of soft, reddish tissue, through which an irregular blood-channel passes. In nearly all cases the vessel-wall is covered with laminated thrombi of varying color and ragged appearance. Where the removal of the thrombi exposes the vessel-wall, it is nearly always found to be extensively diseased (arteriosclerosis) and frequently lacerated.

Internal Changes in Aneurysms.—The dilatation of the blood-vessel takes place with great slowness and is usually followed by further disease of its walls. It is also the immediate cause of some retardation of the blood current. These two factors coöperate to bring about the formation of parietal thrombi, which are deposited layer upon layer until the size of the circulating stream is brought back again to about normal. As the blood-pressure continues to distend the aneurysm and increase its size, more and more fibrin is deposited on the walls. In this way a large mass of thrombi of different ages is formed. When the condition persists for a long time, thrombo-arteritis (*q. v.*) with productive changes occurs, and the process of repair sets in. It is not impossible for aneurysms to recover spontaneously through thrombo-arteritis and the replacement of the thrombi by connective tissue, but as this tendency is opposed to the powerful distending influence of the blood-pressure, the usual course is progressive enlargement and final rupture.

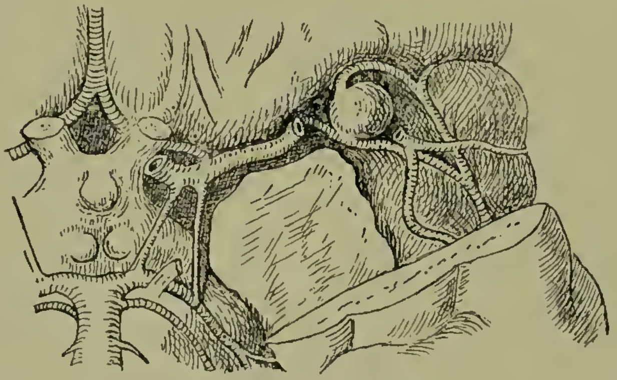

FIG. 245.—Aneurysm of the artery of the Sylvian fossa (Orth).

Spontaneous recovery is possible in aortic aneurysms with very small apertures, but is more frequent in small aneurysms of the smaller arteries. It is not to be expected under any circumstances, however, as the natural tendency of the disease is toward final rupture.

The external changes produced by aneurysms depend upon their progressive growth and the pressure they exert upon the surrounding structures.

The direction taken by an aneurysm in its growth is determined by its point of origin. Unlike an abscess, an aneurysm is not governed by the resistance it meets. When resisting structures impede its growth, it wears them away and continues in its regular direction. For this reason, what will happen in many cases of aortic aneurysm can be predetermined by discovering the point of origin.

Thus, aneurysms of the ascending aorta usually arise a short distance above the sinuses of Valsalva. They are generally small and early rupture into the pericardium, causing sudden death. When arising higher up the ascending aorta, they either project directly forward, become sufficiently large to erode the sternum, and ultimately rupture through the distended superficial tissues of the anterior wall of the thorax, or grow toward the right into the right pleural cavity, into which they finally rupture.

Aneurysms of the arch of the aorta, when situated anteriorly, grow forward and erode the sternum and costal cartilages, or grow backward and erode the spinal column and tissues at the roots of the lung. Aneurysms of the descending aorta usually project toward the left side and grow into and rupture into the left pleural cavity. They may also erode the spinal column.

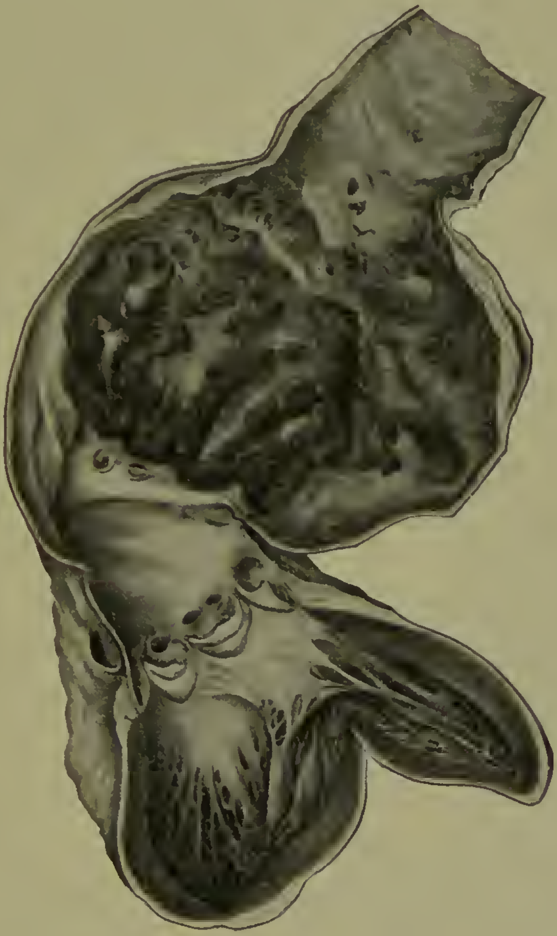

FIG. 246—Aneurysm of the arch of the aorta (Bollinger).

The growth of the aneurysms is, therefore, attended with compression, erosion, and destruction of the important tissues with which they come in contact.

The chief symptoms of aneurysm result from the pressure they exert. Pain of a deep-seated boring character accompanies the bony destruction of the sternum and vertebræ.

The usual termination is rupture, which in aortic aneurysms usually takes place into the right or left pleural cavity, the pericardium, or externally.

Rare seats of rupture are the bronchi, esophagus, stomach, and peritoneal cavity.

Certain of the small arteries, especially those at the base of the brain, are not infrequently subject to *multiple miliary aneurysms* which can be found at autopsy by drawing out the fine vessels with forceps and washing off the adherent brain substance. Charcot and Bouchard found them most frequent in the vessels of the central ganglia, crura, and medulla. The aneurysms are usually situated at the angles of bifurcation. When studied histologically, one finds that the middle coat of the vessel is absent in many cases, and that the remaining walls are thickened and infiltrated with round-cells. Many authorities regard the formation of these aneurysms as a constant precursor of cerebral hemorrhage, and in the cases studied by Charcot and Bouchard, the aneurysms were found in seventy-five consecutive cases. Schmaus cautions us to be careful in regarding all globular enlargements upon these vessels as aneurysms, and points out that in hemorrhagic cases, the very ones in which the aneurysms are most likely to be found, vascular swellings may occur because of the blood from the hemorrhagic focus being absorbed into the adventitial lymph-spaces and thus imitating in appearance minute dissecting aneurysms.

Thrombo-arteritis is an inflammatory reaction of the arteries caused by the presence of a thrombus. Through it the spontaneous cure of aneurysms is in rare cases brought about. Attention has already been directed to the organization of thrombi in the chapter upon Thrombosis in the part of this work devoted to General Pathology.

DISEASES OF THE VEINS.

Because of their superficial position and exposure to traumatic injury, the veins are more liable to disease than the arteries. General morbid conditions may affect both arteries and veins, but show their changes more conspicuously in the arteries. The veins suffer from the effect of gravity upon their thin-walled structures, so that where the circulation is not perfect, there is a marked predisposition to disease of the veins of the lower limbs.

The **fatty degeneration** of the intima and media, which was mentioned under the affections of the arteries, is found under similar conditions in the veins.

Calcareous infiltration occurs in the walls of the veins, especially when diseased. **Amyloid disease** affects the walls of veins and arteries alike.

Phlebosclerosis corresponds to arteriosclerosis, but is not so common. The lesions are similar, except that sclerosis predominates and atheroma is much less frequent. The condition does not predispose to aneurysm because the essential exciting cause—the blood-pressure—is absent. The phlebosclerosis is more common in the veins of the lower limbs, probably because the circulation is weaker and the blood-pressure greater there. The increased connective tissue of the intima not infrequently undergoes calcification. Dilatation of the venous trunks is not infrequently associated with phlebosclerosis. The condition was first pointed out by Rokitansky, and its relationship to arteriosclerosis later explained by Virchow. The morbid anatomy of the condition is almost identical with that of arteriosclerosis, and consists in a proliferation of the connective tissue of the walls, with consequent disappearance of the muscular tissue and a tendency to dilatation from the lessened elasticity. The lesion is said by Birch-Hirschfeld to begin with round-cell infiltration of the subendothelial layer of the intima, hyaline degeneration of its tissue, loss of the muscular-elastic layers, and fibrosis.

The disease usually begins in local areas and spreads until it becomes diffuse or even general, but does not occasion such marked changes as are seen in the arteries. Sometimes the change is discoverable only by microscopic examination. It generally accompanies arteriosclerosis, and, therefore, probably depends upon the same causes.

Phlebitis, or inflammation of the veins, is much more common than arteritis. It may depend upon thrombosis, may be due to traumatism, or may result from the extension of neighboring inflammations to the coats of the blood vessels. It may also be caused by micro-organisms contained in the circulating blood.

Acute purulent phlebitis usually occurs in consequence of purulent or gangrenous disease in the immediate neighborhood of the veins, and begins as a *periphlebitis*. The walls of the vessel become infiltrated with pus, which may extend quite a distance along its length. Sometimes the vessel is actually dissected away from the surrounding tissues by the pus. The intima may or may not take part in the process, and upon this fact will depend the formation of thrombi within the vessel. If the intima remain comparatively normal, the circulation is maintained; if the intima becomes inflamed and roughened, thrombosis is sure to occur. The vessel-wall may become so softened by the purulent infiltration that rupture, with more or less marked hemorrhage, takes place. Before such a condition is reached, however, thrombosis usually occurs and prevents the escape of blood.

Upon the surface of the part the diseased veins show as bluish streaks, which are soft and flexible so long as the circulation continues, but become firm and hard when thrombosis takes place.

Acute purulent phlebitis sometimes originates as *endophlebitis* from infectious agents in the form of pus-cocci, etc., in fragments entering the vein from diseased tissues. In such conditions there is an exudation of serum and leukocytes from the vasa vasorum and a marked infiltration of the walls, while, at the same time, thrombi form within. One of the best examples of this process is the so-called *milk-leg*.

The termination of acute phlebitis must depend upon the extent of the damage done. In periphlebitis the pus formed may escape externally and the vessel itself show comparatively little change, but if thrombosis has occurred, thrombophlebitis must take place and the vessel be obliterated.

Thrombophlebitis, or inflammation of a vein from the presence of a thrombus, is common because of the frequency of venous thrombosis. It is most frequent in the veins of the pelvis and lower extremities.

The process is identical with thrombo-arteritis, already described, and leads to **phlebitis obliterans**. When the thrombi only partially organize, the remaining, centrally situated portion is apt to calcify and form a freely movable calculus,—*phlebolith*,—which can usually be driven up and down the veins for a short distance with the fingers, though sometimes firmly attached. These bodies seem to be most common in the dilated veins seen in many pelvic diseases.

The unfortunate sequels that follow arterial obstruction—necrosis, gangrene, and death—are much less frequent in venous obstruction, because of the facility with which collateral circulation can be established.

Syphilitic Phlebitis.—Syphilis in infants seems to be a common cause of endophlebitis of the umbilical vein, and may lead to considerable stenosis, and Hübner found similar changes in the veins of the lower extremities of syphilitic adults. Schüppel has described a pylephlebitis syphilitica of infants. Gumma of the veins occasionally occurs, and is a cause of phlebitis obliterans. Syphilitic phlebitis is perhaps most frequent in the branches of the portal vein.

Tuberculous phlebitis and periphlebitis occur exactly as do the similar diseases of the arteries. By extension of the process so that the softened tubercles open into the lumen of the vein, tubercle bacilli may gain entrance into the blood-stream and cause disseminated miliary tuberculosis.

Phlebectasia, Varix, or Varicose Veins.—Phlebectasia, or dilatation of the veins, is a common condition.

Etiology.—In some cases it seems to be an inherited weakness of the vessel-walls. It is more common among Caucasians than other races, and among women than men. In many cases the conditions predisposing to dilatation are to be found in the vein itself, as local or general phlebitis or phlebosclerosis, under which circumstances the phlebectasia bears an exact parallelism to the dilatations of arteries. The pressure of the blood is the actual distending force, and the dilatations are most frequent where venous pressure is exerted. For this reason it is most common in the lower limbs, and is almost invariable in weak heart with venous engorgement, and in enfeebled circulation from other causes. Lack of exercise also favors it. Pressure upon the venous trunks by morbid growths, aneurysms, etc., and obstruction by cicatricial tissue, as in cirrhotic hepatitis, venous thrombosis, phleboliths, etc., all favor its development.

Morbid Anatomy.—The dilatation may be cylindric, the entire vein being dilated, or may be saccular, the enlargement being circumscribed and located near the valves. If the increased length of the vein causes it to become tortuous or spiral, it is spoken of as *cirsoid.*

In cirsoid phlebectasia the windings of the tortuous vessels not infrequently come in contact with each other, unite by inflammatory adhesion, and later suffer pressure atrophy of the walls, by which they subsequently communicate. Such communications are called *varices*, or *varix*. When the dilatation embraces a considerable number of veins, which become considerably widened and have frequent communications with each other, a cavernous tissue somewhat resembling erectile tissue, and not always easily differentiated from angioma, is formed. The dilatation brings about thinning of the wall of the vessel and further yielding, and leads to periphlebitis, sometimes followed by the formation of a dense, cavernous, cicatricial tissue which has little vitality, and when injured, is apt to ulcerate. The skin is also liable to be embraced in the chronic inflammatory condition, and on the lower limbs a chronic eczema is commonly observed in association with varicose veins.

In the veins, especially when inflamed or injured, thrombosis, followed by thrombophlebitis, obliteration, or phlebolith formation, may occur. It is partly because of this thrombosis and obliteration that hemorrhage from rupture of the dilated veins is prevented.

Varicose veins are most frequent in the lower extremities, the hemorrhoidal, spermatic, and pelvic veins.

Special names are sometimes applied to dilatations of certain groups of veins; thus, when the spermatic veins are affected, the condition is described as *varicocele;* when the hemorrhoidal veins are affected, as *hemorrhoids* or *piles*.

Hemorrhoids are dilatations of the branches of the hemorrhoidal veins which project upon the surface of the mucous membrane of the rectum near the anus and upon the adjacent skin, in the form of small, single or multiple tumors varying in size from a pin-head to a marble. They are usually soft, elastic, or spongy in consistence, and may be sessile or pedunculated. The condition is most often encountered in those who lead sedentary lives or suffer from diseases which are accompanied by obstructions of the portal system, as cirrhosis of the liver. They not infrequently accompany other venous dilatations. They are called external and internal, according as they occur within or without the external sphincter muscle.

The passage of the feces over hemorrhoids not infrequently causes minute lacerations of their surfaces, or so increases the pressure upon them that they bleed quite freely. They also occasionally rupture beneath the skin, and not infrequently become infected and suppurate. Tuberculous infection occasionally occurs, and may lead to fistula in ano. Thrombosis with thrombophlebitis is common, and transforms the hemorrhoids into simple fibrous tumors. External hemorrhoids are less painful and less serious than internal hemorrhoids, and bleed less, because of their thicker covering of skin or stratified squamous epithelium. Internal hemorrhoids of long duration are apt to become covered by squamous epithelium through metaplasia of the columnar epithelium of the rectum.

DISEASES OF THE LYMPHATIC VESSELS.

Lymphangitis, or inflammation of the lymphatic vessels, is almost always a secondary affection of micro-organismal origin. The inflamed vessels appear to the naked eye as indefinite red streaks extending from the inflamed part in the direction of the lymphatic circulation, sometimes for long distances. In cases of felon and infected wounds of the hands followed by lymphangitis the vessels are inflamed to the elbow or even to the axilla. The vessels are not usually palpable, but are sensitive to pressure.

The structural alterations may be very simple. consisting of the collection of lymph in the vessel, the presence of the micro-organisms, a tendency for the endothelial cells to swell, assume a more spheric shape, and proliferate or degenerate, according to the severity of the infection.

There may be more or less coagulation of fibrin in the vessels in some cases, and in others, in which the condition is suppurative, the vessel may be filled with pus-cells. The redness seen upon the surface of the skin depends upon associated *perilymphangitis*. The facility with which the condition recovers will depend upon the severity of the attack. Mild cases easily regain their normal status, while suppurative cases may lead to the total disorganization of the vessel. Such obliteration is of little consequence because the collateral lymphatic circulation is so easily established. Indeed, obliteration of the largest lymphatic trunks and even of the thoracic duct itself may produce no important changes.

Dilatation of the lymphatic vessels or lymphangiectasis is of not infrequent occurrence. It is seen in cases of lymph-scrotum and elephantiasis, and may be due to the obstruction of the lymphatic vessels by parasites. The chronic engorgement of lymphatic systems resulting from this condition leads to a massive proliferation of the surrounding connective tissue, as is seen in *elephantiasis*.

The lymphatics of the mesentery—especially the lacteal vessels—not infrequently dilate. Occasionally the small lymphatic vessels of the peritoneum and pleura dilate and appear as small, rounded points, not unlike miliary tubercles, upon their respective membranes. When these are incised or punctured, clear lymph escapes.

Tuberculosis of the lymphatic vessels is frequent in all forms of tuberculosis, but particularly so in tuberculosis of the serous membranes. Tuberculous lesions of the pleura are commonly associated with a cheesy infiltration and tubercle formation of the lymphatic vessels, which appear as grayish streaks or cords upon the surface of the costal pleura.

CHAPTER III.

DISEASES OF THE DIGESTIVE SYSTEM.

DISEASES OF THE MOUTH AND ITS ASSOCIATED PARTS.

THE mouth is frequently the seat of traumatism and infection. Into its cavity the food is introduced in every condition of crudity and refinement, boiling hot or freezing cold, and subjected to one of the most violent of the body's physical processes, mastication. In it fragments remain after the food is swallowed, forming excellent nutriment for myriads of bacteria which habitually reside there. A score of different micro-organisms habituate the oral cavity, among them being the cocci of suppuration. Taking these facts into consideration, it is remarkable that our mouths are not constantly injured and infected, instead of only occasionally so.

THE LIPS.

The *lips* are subject to a few primary lesions and to numerous secondary affections extending from the neighboring skin of the face and mucous membrane of the mouth. Of the primary affections, the most simple is the mild catarrhal inflammation known as "chapped lips." This depends upon the influence of dry air upon the delicate epithelial structure, which becomes hyperemic and thickened and has a tendency to detach in shreds and lamella, leaving the more deeply seated cells exposed and predisposing to subsequent oozing and drying, with the formation of crusts. The changes may go deeper than the epithelium and cause fissures and ulcers situated chiefly in the center of the lower lip or at the corners of the mouth. Such *rhagades*, as they are called, are very painful at times. More serious is true **cheilitis,** in which the described changes are intensified, and in which the rhagades not infrequently become infected and lead to suppurative and phlegmonous inflammations.

A *chronic cheilitis* is occasionally seen in children of strumous or scrofulous diathesis. It results in thickening of the upper lip, which becomes misshapen in consequence and often presents rhagades and ulcers. Such lips are commonly associated with enlarged lymphatic glands in the neck and other signs of tuberculosis.

THE MOUTH.

Inflammation of the mouth is described as **stomatitis.** It depends upon external and internal conditions, but local infection from the ever-present bacteria is most common and important. The severity of the process varies from simple erythema to gangrene. It is usual to describe catarrhal, ulcerative, mycotic, and gangrenous stomatitis.

1. **Catarrhal Stomatitis.**—This is the commonest and mildest form. A simple primary erythema changes into a deep-red or livid hyperemia. The tongue, lips, cheeks, and other soft tissues are most affected, while the hard palate and the tissues of the alveolar processes swell less and show less congestion. The tongue is large and nodular on the surface from enlargement of its papillæ. The salivary glands are unusually active, and the saliva from

the mouth contains a large number of desquamated epithelial and some pus-cells. False membranes, consisting of desquamating epithelium, bacteria, pus, and saliva, sometimes form on the lips and tongue.

The disease is caused by mechanical and chemic irritants, carious teeth, the introduction of irritating foods, excessive indulgence in tobacco and alcohol. It also not infrequently occurs in children during dentition.

The disease is not always dependent upon local causes, but may occur in a slightly different form in such specific infectious diseases as measles, small-pox, chicken-pox, etc. Erysipelas has also been known to extend into the mouth.

Catarrhal stomatitis is rarely symmetric, being most frequently an extension of a local infection.

2. **Ulcerative Stomatitis.**—This form of inflammation of the mouth is more frequently seen in children than in adults, and seems to occur in persons of reduced vitality. It is observed in general malnutrition, tuberculosis, diarrhea, typhoid fever, diabetes and scurvy, and in phosphorus, mercury, and other mineral poisonings.

The disease begins in the gums, which become red, swollen, and loosened, so that they resemble cushions from which the teeth scarcely project. The swollen gums bleed easily upon the slightest injury. As the disease progresses, the borders of the gums begin to change in color and appearance and are transformed into a softened, lacerable, yellowish, necrotic mass, which, when intentionally or accidentally removed, leaves a bleeding surface which becomes an ulcer.

The ulcerative changes are usually first noticed upon the gums of the front teeth and spread laterally, though not always symmetrically. Once established, the inflammatory conditions are not limited to the gingival tissues, but may spread to the cheeks, the lips, the tongue, or the tonsils. The superficial tissues are chiefly affected, but the disease may spread to the periosteum, and periostitis, ostitis, and even necrosis of the alveolar processes may occur, the teeth not infrequently falling out. The disease is acute, and in most cases recovers perfectly, though bad cases may hasten death in patients suffering from preëxisting tuberculosis, etc.

When ulcerative stomatitis depends upon lead-poisoning, a blue line usually appears upon the gums at the edges of the teeth.

Systemic conditions have much to do with the primary changes in the gingival tissues, but the chief lesions of the affection seem to result from multiple local infections.

When mercurial poisoning (salivation) was a common result of therapeutic mismanagement, the occurrence of ulcerative stomatitis was much more frequent than at present.

3. **Mycotic Stomatitis.**—This is a form of oral inflammation distinctly and primarily micro-organismal in character. Aphthous or follicular, diphtheric, and oïdium stomatites are typical examples.

(*a*) *The Aphthous or Follicular Stomatitis.*—This form of oral inflammation is chiefly seen in children suffering from marasmus, digestive and general febrile disorders, though occasionally in adults under similar conditions.

It is characterized by the presence of small, multiple, disseminated areas of inflammation (*aphthæ*), which may be found upon the tongue, lips, cheeks, or palate, more rarely upon the gums. The patches are irregularly rounded or elongate, surrounded by a livid red zone, and are yellowish-white in color and opaque.

The *aphthæ* are areas of local infection, the exact cause of which has not been made out. There is probably no specific infectious agent.

A study of their structure has caused E. Fränkel to regard them as croupous inflammations, because, together with destroyed epithelium, a network of hyaline fibrin filaments and masses can be observed in the connective tissue.

The disease is subacute, lasting for weeks, the aphthæ occurring in successive crops and healing slowly by a gradual absorption of the exudate and regeneration of the epithelium. The inflamed points are very painful, so that the disease becomes serious in conditions of associated malnutrition, because the patients cannot eat.

(*b*) *Diphtheric Stomatitis.*—Diphtheria of the mouth is usually a complication of pharyngeal diphtheria, which reaches the oral cavity by extension through the posterior nares and along the palate. Occasionally it occurs primarily upon the tongue or cheeks, and may then be unilateral or bilateral.

Non-diphtheric pseudomembranous stomatitis in most cases results from the ingestion of caustic substances. Occasionally, however, it seems to be mycotic or bacterial.

(*c*) *Oïdium stomatitis,* also known as *thrush,* is a peculiar mycotic inflammation of the mouth occasionally seen in infants, and characterized by the presence of a specific micro-organism, the Oïdium albicans.

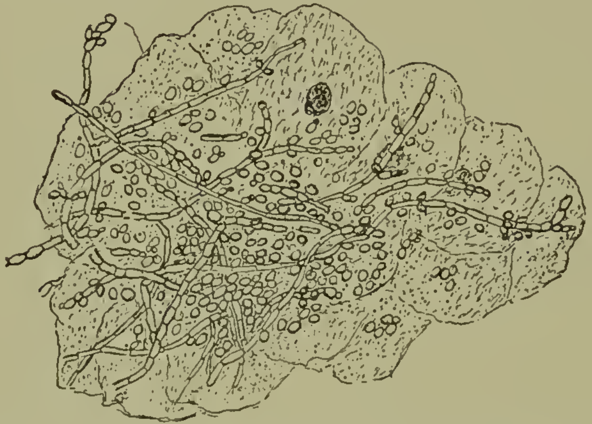

FIG. 247.—A group of vaginal epithelial cells overlaid by mycelial threads and conidia of Oïdium albicans (Smith and Radkey).

The lesions are usually situated upon surfaces normally covered by transitional squamous epithelium, the tongue being most frequently affected. The contact of the tongue with the roof of the mouth may cause secondary infection of the palatal tissues. Infants and marasmatic adults are affected, the disease not being very common even in those whose vitality is considerably depressed. Adults suffering from the last stages of tuberculosis are sometimes infected.

The lesions of the disease begin with diffuse reddening of the mucous membrane and the formation of a somewhat shining, slimy, adhesive layer of grayish-white matter, which is said to have an acid reaction. As the disease develops, whitish dots are seen to appear upon the surface and gradually spread, sometimes coalescing. This white formation characterizes thrush. It is in reality a pseudomembrane made up essentially of detached epithelial cells with a ramifying network of parasitic threads. The white color of the patches contrasts markedly with the hyperemic surrounding tissues. When the patches are removed, they speedily reappear upon the abraded surface. In severe cases the disease is not confined to the tongue, but spreads to the palate, lips, pharynx, esophagus, and, in spite of the columnar epithelium of the stomach and intestines, has been seen to involve these tissues. From the local lesion the parasites are sometimes metastatically transported to other parts of the body. Such mycotic embolism may occur in any organ, and has been known to cause death when occurring in the brain.

Ordinarily the disease is not serious, but it may be a cause of death when the pain it causes prevents the taking of food.

The Oïdium albicans is one of the budding fungi, and seems to be properly classified near the yeasts. It occurs in the form of rounded, oval, or cylindric cells, 3.5 to 5 μ in diameter, and ten or twenty times as long as thick, which bud and extend in all directions, forming what appears to be a reticulum by remaining attached to each other. Some of the cells are so elongate as to resemble the mycelial threads of the higher fungi. Spores are formed, occurring singly in round-cells. The fungi are chiefly seen in the epithelial tissue, but as the cells degenerate in consequence of the disorganization of the tissue, they may enter the areolar tissue and cause a deeper form of inflammation.

The micro-organism is easily isolated and cultivated upon artificial media. Upon acid, sugar-containing substances the little plant appears most like the yeasts, though when cultivated upon alkaline media, it forms longer threads suggestive of the mycelia of the fungi.

The vegetation of the micro-organism gives rise to a pure white colony upon agar-agar and upon potato.

The micro-organisms can be well stained by Gram's method. Usually there is little difficulty in differentiating between thrush and diphtheria or the aphthous form of stomatitis.

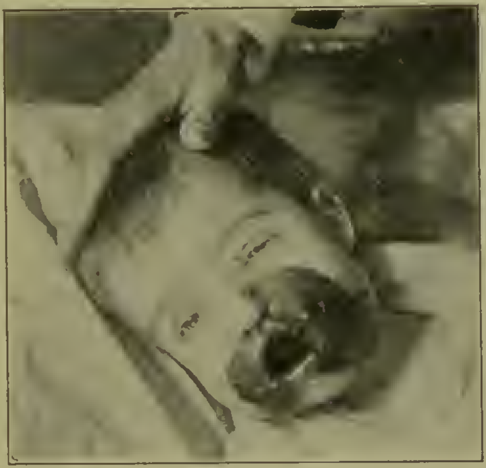

FIG. 248.—Noma of the face (case of A. T. Bazin).

4. **Gangrenous Stomatitis.**—The most serious infection of the oral tissues is gangrenous stomatitis, or *noma*. The disease is, fortunately, rare. It affects children between two and twelve years of age, especially those whose nutrition is depraved and who have been exposed to extremely unhygienic surroundings. It is usually a primary affection, but sometimes follows ulcerative stomatitis, and may follow measles and typhoid fever. In adults it occasionally succeeds malaria. The most common point of infection is the buccal mucous membrane of one side (rarely both) near the angle of the lip. The lesion forms a livid, swollen area, which is rapidly followed by gangrene. The center of the patch may become grayish-yellow before gangrene actually sets in.

The gangrene may extend entirely through the cheek, or may be limited to the mucous membrane and subjacent tissue. When the extension to the skin takes place, a purplish spot appears upon the cheek, vesication soon follows, and the tissue melts into a fetid, pultaceous mass. The disease is commonly fatal from exhaustion and secondary infection. When recovery takes place, it is through separation of the sphacelus and subsequent cicatrization. Considerable deformity invariably follows contraction of the scar. Noma also occurs about the genital organs.

The most recent investigations indicate that though streptococci and other micro-organisms are possibly responsible for the violence and gangrenous nature of the process, it is really the diphtheria bacillus, which is always present, that is responsible for the disease by opening the tissues to their activity.

5. **Syphilitic stomatitis** is far from uncommon. The primary sore, the chancre, is sometimes situated in the mouth, and may take either a soft or an indurated form, and be accompanied by lymphatic enlargements. The *primary* syphilitic oral lesions are usually situated upon the tongue or lips. Secondary lesions (mucous patches), which are far more common, are seen upon the gums and at the angles of the mouth. They take the form of superficial ulcerations following cellular infiltrations. Flat, superficial, slightly prominent, grayish-yellow patches seen upon the tongue or other parts of the mouth of syphilitics are known as *leukoplakia syphilitica*.

Small papules sometimes form upon the mucous membrane, appearing as slightly elevated, bluish-white or pearl-colored patches, surrounded by a red zone. These are described as *opaline plaques*. These are most common upon the lips, cheeks, tongue, and soft palate.

Of the tertiary lesions, the *gumma* of the mouth is usually quite small, varying from the size of a lentil to that of a bean. Softening and evacuation lead to ulceration and cicatrization of the mucous membrane.

Syphilitic cases not infrequently suffer from atrophy of the mucous membrane of the base of the tongue, with loss of the circumvallate papillæ, but this also occasionally takes place in non-syphilitic individuals.

6. **Tuberculosis** of the mouth is nearly always secondary, resulting from the passage of sputum, etc., containing the tubercle bacillus, through its cavity. It may also depend upon lupus of the face. The posterior portion of the tongue is most frequently attacked. Rarely one finds the lesions upon the cheek, jaws, and lips. The tubercles almost always occur as isolated, yellowish-red nodules or ulcerations. In a few cases confluent tubercles have been seen. When ulcerations occur, they are irregularly formed and usually possess overhanging edges.

Primary tubercles of the mouth have been seen upon the mucous membrane of the lips and cheeks, and also upon the tongue. The infection in these cases seems to depend upon infection from substances taken into the mouth.

It may depend upon direct infection by the kiss of a consumptive or the use of his cigar-holder, pipe, fork, etc. The nature of the primary tuberculous lesion may be difficult to determine. There is usually an ulcer of some size, irregularly excavated, and surrounded by overhanging indurated edges. Outlying tubercles may or may not be present. The appearances are not at all unlike those of the gummatous ulcer.

Actinomycosis of the tongue is not infrequent in cattle. The inoculation possibly takes place through inconspicuous lesions made by the spines of certain grains. The fungus develops in the tissues and produces the lesions already described. (See p. 347.) In chronic cases the tongue becomes hard or "wooden"; in the more acute cases it is filled with small areas of suppuration and sinuses.

THE TONGUE.

Glossitis, or inflammation of the tongue, may be superficial or deep.

(*a*) The **superficial form** is catarrhal in character and results in denudation of the surface. If the patient keeps the tongue quiescent, so that friction against the teeth does not remove the desquamated cells, its surface becomes covered with a white coating consisting of cells and bacteria. If this still is undisturbed, and if fragments of food are added to the general mass, the bacteria grow still more plentifully, and the layer increases in thickness and becomes grayish-yellow and later brownish, dry, hard, and firm, while the tissue of the tongue becomes fissured and cracked.

Various grades of the process are observed in smokers, dyspeptics, and those in the typhoid state.

Occasionally the superficial inflammations of the tongue become chronic and characterized by the formation of local thickenings of the mucous membrane—*leukoplakia* or *psoriasis linguæ*.

(*b*) The **deep inflammations** of the tongue depend upon injury and infection. The organ, according to the degree of the disease, becomes swollen, hard, and painful. The tissues are congested and infiltrated with leukocytes. There may be atrophy or degeneration of the muscle-fibers, and abscesses may form. The most frequent cause is infection from carious teeth.

Syphilitic and tuberculous lesions of the tongue have already been described.

A peculiar and interesting pathologic change, sometimes occurring in the tongue, is an abnormal development of the epithelium upon the papillæ, which leads either to a nodular tongue or to a hairy or bristly tongue, according to whether the fungiform or the filiform papillæ are affected. Under these circumstances the tongue may become discolored and appear brown or green, the condition being described as a "*black, hairy tongue*."

The **tumors** of the mouth are important. **Lymphangioma** and **hemangioma** of the tongue and lips are common in early life. They are usually simple, and most frequently situated in the upper lip or beneath the tongue. The hemangioma is characterized by a bluish or purplish color.

Connective-tissue tumors are not infrequent in early life, and **lipoma, fibroma, myxoma,** and **sarcoma** are occasionally observed.

Teratoid tumors are not uncommon in and about the mouth.

Sarcoma, carcinoma, and **epithelioma** occur in later life. The first mentioned is not infrequent upon the gums about the roots of the teeth, and is known as *epulis*. All epuli are not sarcomatous, however, as it is not rare to find them purely fibrous, and, indeed, Sutton restricts the term to fibrous growth. Occasionally the epuli grow from other parts of the jaws than the alveolar processes. Their general appearance is that of firm, rounded, nodular tumors. Sometimes they are of bony origin, and present the histology of osteosarcoma or giant-cell sarcoma. Such forms usually develop near the symphysis mentis. Papillomata are common upon the lips at their edges.

Cancers of the mouth are most frequent upon the lips, tongue, and gums, and are chiefly of the squamous variety. They first appear as circumscribed, rather firm, grayish-white swellings upon the epithelial surfaces, which become more and more apparent as the growth advances. When softening sets in, ulcerations are formed and show little disposition to heal. The course of epithelioma of the tongue is particularly rapid and malignant.

Adenoma sometimes develops from the mucous glands of the mouth, and Ziegler mentions the occurrence of thyroid-gland tumors in the course of the thyrolingual duct.

Cysts.—The most frequent cyst of the mouth is the so-called *ranula*. Almost any cyst of the mouth is called by this name, but the true ranula results from dilatation of the ducts of the Blandin-Nuhn's glands situated beneath the tip of the tongue. Nearly all the oral cysts are retention cysts caused by obstruction of the glandular outlets, either of the larger glands, or of the little mucous glands so common in the mucous membrane. Occasional dermoid cysts are found.

THE TONSILS.

The tonsils occupy a part of the throat predisposed to inflammation and infection. Thus in nearly all the catarrhal inflammations and in diphtheria of the pharynx the tonsils are always more or less involved because of their proximity.

The primary affections of the tonsils are really few, though the appearances vary, and numerous names have been applied to them. For convenience they are probably best divided into the *acute* and *chronic* tonsillitis.

Acute tonsillitis is sometimes an idiopathic affection, depending upon accidental infection by bacteria entering the crypts. It also not infrequently accompanies exanthematous diseases, and though the relationship is not clear, occasionally precedes rheumatism. The inflammation is usually superficial, the organs becoming swollen, hyperemic, and bright red. The surfaces are covered with an abundant secretion of seromucus, which pours from the lacunæ. As in most tonsils the lacunæ are rather large and conspicuous, and as in most tonsillar inflammations they contain and discharge an abundant secretion, which often becomes inspissated and appears creamy or cheesy, the majority of the acute tonsillites are spoken of as *lacunar* or *follicular*. The morbid anatomy is extremely simple, there being no changes excepting those depending upon the congestion and increased secretion. A variety of bacteria can be cultivated from the crypts of the tonsils, of which the streptococcus may be the most important. Both tonsils are usually symmetrically affected, which would perhaps indicate that something more than the accidental entrance of bacteria is required for the development of the disease, as it would be difficult for accidental infection to occur simultaneously in both organs.

In less common cases, in which a deeper infection occurs, the inflammation may advance to suppuration, usually in one, but sometimes in both, tonsils. When this occurs, the condition is described as *suppurative tonsillitis* or *quinsy*.

Herpetic tonsillitis occurs rather infrequently, and chiefly in individuals predisposed to herpes. It is characterized by an eruption of minute vesicles upon the mucous membrane, with the addition of catarrhal inflammation. The herpes vesicles rupture and leave painful ulcers.

Chronic tonsillitis varies in its morbid changes. In some cases the effect of the disease is chiefly seen in the crypts, which become much larger than normal, are of unusual depth, and serve as collecting places for secretions, desquamated epithelial cells, bacteria, and fragments of food. The bacteria in these accumulations bring about putrefactive changes, which in turn increase the irritation of the surrounding tissue.

When such tonsils are examined, yellowish-white, fetid, more or less firm masses, varying in size from a rice-grain to a pea, are seen projecting from them. The breath of the patient has a very unpleasant but quite characteristic odor. The masses escape spontaneously from time to time, or may be retained, when they sometimes calcify and form concretions or *calculi* in the tonsils.

This form of chronic tonsillitis, because of the increased size of the lacunæ, which enlarge at the expense of the tonsillar tissue, may be described as *atrophic*.

Other cases of chronic tonsillitis are *hypertrophic*, and lead to marked enlargement of the organs, which project from between the pillars of the fauces, so as nearly to meet in the mesial line, and form serious obstacles to deglutition, respiration, and enunciation.

The enlargement seems to be a true hypertrophy, and consists of hyperplasia of all the constituent tissues of the organ. When examined, the organ seems normal, except that it is very large and slightly reddened on the surface. The crypts are small and the surfaces smooth.

The tonsillar enlargements sometimes depend upon chronic inflammation and sometimes are associated with general increase of the lymphadenoid tissue of the pharynx, in which numbers of the so-called "adenoid vegetations" occur upon the pharyngeal walls. Enlargement of the tonsils also occurs in leukemia.

Tuberculous infection of the tonsils, with secondary extension to the cervical lymphatic glands, is probably much more frequent than is usually supposed.

The fact that the crypts of the tonsils contain lymphoid tissue which comes in actual contact with the surface makes it easy to explain the facility with which infection can occur. Though tuberculous infection of the cervical glands may depend upon infection through the upper part of the respiratory apparatus, it is also true that alimentary infection may occur through the tonsils. There is experimental evidence of this, and young pigs fed upon tuberculous milk have been found to acquire tuberculosis of the tonsils, with early infection of the cervical glands.

Pseudomembranous tonsillitis may or may not be *diphtheritic*.

(*a*) *Tonsillar diphtheria* depending upon the Klebs-Löffler bacillus usually begins with the formation of a grayish-yellow pseudomembrane about the edges of the lacunar openings and upon the surface of the organ. So similar is this pseudomembrane to that of the non-diphtheritic form that only by a bacteriologic examination can they be certainly differentiated.

(*b*) *Streptococcus inflammation* of the tonsil is sometimes accompanied by the formation of a distinct pseudomembrane in all general appearances identical with true diphtheria, though usually the membrane is whiter, less intimately attached, and its occurrence accompanied by more profound constitutional disturbance.

THE PHARYNX.

Acute catarrhal pharyngitis is one of the most common affections.

Etiology.—Its cause is not satisfactorily determined. It often seems to follow exposure to cold. It may, however, signify that there has been an invasion of the body by micro-organisms. It seems at times to follow attacks of indigestion and result from the absorption of leukomains, and at other times certainly depends upon the inhalation of irritating substances, such as tobacco-smoke and dust.

It is scarcely possible for the pharynx to be inflamed without a sympathetic affection of the soft palate and tonsils. For this reason many prefer to use the term *angina* as descriptive of the acute affections of these parts.

Morbid Anatomy.—The acute pharyngitis is extremely simple in its morbid anatomy. The chief manifestations are redness and swelling of the mucous membrane of the part, with a primary cessation of the normal secretion, which causes the throat to feel very hot and dry, and later an overabundant secretion of the mucous or mucopurulent matter, which may at times be mixed with a little blood, and which, as it clings tenaciously to the surface, is removed by the patient with considerable effort. When the secretion is examined with the microscope, it is found to contain many pus-cells and many desquamated and degenerated columnar epithelial cells from the pharyngeal walls.

When, in severe cases, the posterior wall of the pharynx is examined, red, abraded areas of irregular size and shape are found. These are true abrasions. There are also rounded or oval, distinctly circumscribed, slightly elevated, red areas which are small collections of lymphoid tissue made unusually conspicuous because of the degree of congestion present.

The disease is of short duration and ends in recovery. It has, however, a marked tendency to recur and become chronic.

Chronic Pharyngitis.—The chronic disease follows repeated attacks of the acute disease, though it may occur independently and is very common as the result of the abuse of tobacco. There is chronic congestion of the part, the adenoid-tissue collections become prominent, and the secretion becomes very meager and may be absent. When present, it may be mucopurulent or purely mucus. It sometimes partly inspissates, especially in the nasopharynx, and begins to decompose, imparting a foul odor to the breath. The cases are divided into the *productive* forms (pharyngitis hyperplastica), in which papillary projections and excrescences may develop in the pharyngeal walls, and the *atrophic* forms (pharyngitis atrophicans), in which the mucous membrane appears relaxed, thin, red, and smooth. It is possible for both processes to exist at the same time, for the hyperplasia is not so much a thickening of the mucous membrane as it is an increase in the lymphadenoid tissue it contains. The pharyngeal tonsils are particularly disposed to increase in size and may greatly interfere with breathing.

The mucous membrane over the adenoid hyperplasias may be thinned and is not infrequently ulcerated.

Pseudomembranous pharyngitis is characterized by the formation of a yellowish-white or yellowish-gray layer upon the mucous membrane, and may be *diphtheric* or *non-diphtheric.*

Non-diphtheric pseudomembranous pharyngitis may result from the action of various injurious agents, which may be taken into the mouth and swallowed (steam, ammonia, etc.), but is nearly always dependent upon the activity of bacteria. The chief cause is the Streptococcus pyogenes, though pneumococci, colon bacilli, and other organisms may cause it.

Taking the streptococcus pseudomembranous inflammations first, we find them in association with certain of the exanthematous diseases, notably scarlatina, measles, small-pox, and typhoid fever. They may, however, occur as primary affections.

In addition to the streptococci, etc., it is customary to find a number of the organisms belonging to the flora of the mouth, so that nearly every case is one of mixed infection.

It is impossible to distinguish, without the aid of a bacteriologic examination, between diphtheric and non-diphtheric pseudomembranous pharyngitis. This is an important matter, and has a great bearing upon diagnosis, prognosis, treatment, and hygiene, for when such an examination proves the case to be one of true diphtheria, irrespective of the apparent gravity of the case, the contagious nature of the disease, the indication for the use of the diphtheria antitoxin, and the fear of future palsy are all at once opened up. On the other hand, if such an examination shall show the presence of streptococci and the absence of the diphtheria bacilli, the mind of the physician is relieved, and he knows that the case is not contagious and will not be followed by palsy.

Diphtheritic pseudomembranous pharyngitis is caused by the true diphtheria bacillus, the Klebs-Löffler bacillus, a brief mention of which will not be out of place.

It was discovered by Klebs in 1883, and cultivated by Löffler in 1884, and in consequence is known as the Klebs-Löffler bacillus. It is a rod-shaped bacillus with round ends, and stains well with ordinary staining solutions, but most characteristically by the alkaline methylene-blue of Löffler. It also stains well by Gram's method, especially when in sections of tissue.

The bacillus has a variable morphology, appearing very different upon different media and in differently reacting media. It thus varies from a short oval, which quite habitually occurs in pairs in bouillon, to an enormous, club-shaped bacillus when grown upon alkaline blood-serum. It varies thus not only in shape, but also in size.

It is not motile and has no flagella. In specimens stained with the alkaline methylene-blue solution one sees a marked tendency to segmentation, and a pronounced disposition on the part of the bacillary substance to color irregularly, either at the poles or at various points along the length of the organism. The bacillary substance thus contains polychromatophilic granules.

The bacillus grows in all culture media. The most characteristic growth is upon Löffler's blood-serum mixture (3 parts of serum plus 1 part of 1 per cent. glucose bouillon), which is employed in all laboratories for the diagnosis of diphtheria. Upon it the organism grows so rapidly that in from twelve to twenty-four hours the surface is dotted with small, china-white or yellowish-white colonies, or covered with a continuous layer of the same color, accordingly as the number of bacilli distributed upon the surface has been few or many and the duration of growth long or short. It is possible to make a diagnosis of diphtheria by the use of this medium in five hours.

The diphtheria bacillus does not liquefy gelatin. In its growth it first produces acids by transformation of the contained sugars, then forms alkalis, which later neutralize and predominate over the acidity. The organism is toxic. Different bacilli—*i. e.*, bacilli from different sources—vary greatly in their ability to produce toxin, and the production of toxin is the only criterion for the separation of the true diphtheria and pseudodiphtheria bacilli. The bacillus is pathogenic for most of the laboratory animals. Rats are immune. When inoculated, the animals usually die on the third day from the effects of the intoxication. At the sight of inoculation there is a fibrinohemorrhagic exudate.

Morbid Anatomy.—As there is no difference of importance in the naked-eye appearance between the streptococcous inflammation of the throat and true diphtheria, the morbid anatomy of both forms of pseudomembranous angina can be described as though they were identical.

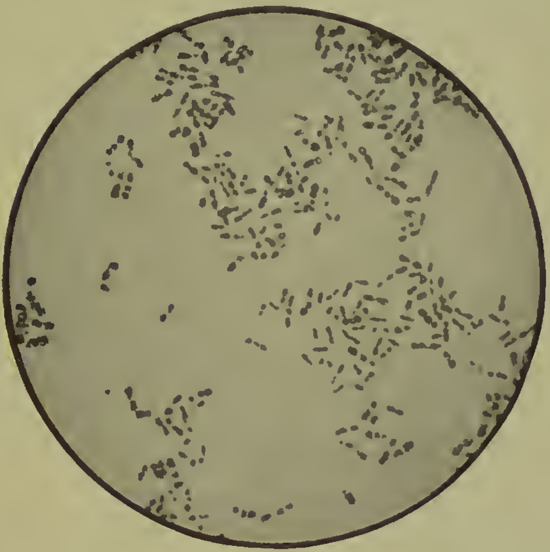

FIG. 249.—Bacillus diphtheriæ, from a culture upon blood-serum; × 1000 (Fränkel and Pfeiffer).

The extent of tissue invaded by the pseudomembrane varies. The disease may begin upon the pillars of the fauces, upon the tonsils, or upon the sides of the uvula, and remain localized, or may spread so that the entire pharynx, nose, and mouth become affected, and the disease eventually reaches the lips and anterior nares.

The characteristic lesion is the pseudomembrane. It is of a whitish, yellowish, grayish-yellow, or dirty-gray color, and forms upon the surface of the mucous membrane of the affected part. It usually forms a single layer of moderate thickness, but occasionally there may be several layers, and it is sometimes quite thick. The edges of the membrane may be indistinct, gradually fading into the surrounding healthy tissue, or may be distinct and even detached, this depending upon the stage of the disease and its tendency to further extension and exfoliation. The membrane is not very adherent, as a rule, but can be divulsed, leaving an abraded surface upon which a new membrane quickly forms.

The streptococcous pseudomembranes are usually whiter in color than the diphtheric membranes, and seem to form upon a more acutely inflamed surface. Streptococcous inflammations are apt to be more painful than diphtheria, and may be equally fatal. A bacteriologic examination is the only certain means of differentiation, and is important, as only the true diphtheria is contagious and remediable by the antidiphtheric serum.

In cases of true diphtheria which have been treated by vigorous use of the serum, the edges of the membrane are outlined by a distinct zone of hyperemia. Streptococcous inflammations are prone to begin in the crypts of the tonsils and spread about the edges of the crypts.

The usual point from which diphtheria spreads is the arch of the fauces. The membrane forms upon the posterior pillars and sides of the uvula, extends over the tonsils, and climbs into the nasopharynx and down the posterior pharyngeal wall. It may descend into the larynx, go on into the trachea, and even into the bronchi. It commonly passes into the nose, and Osler performed an autopsy upon a case in which the whole mouth being full, the membrane extended beyond the lips upon the skin.

The membrane consists of an inflammatory exudate whose chief ingredient is fibrin. As this exudate occurs, it coagulates among the superficial cells of the mucous membrane and brings about coagulation necrosis of all the superficial tissues. This early necrosis of the superficial tissues allows the diphtheria bacilli to come in contact with the subjacent areolar tissue, upon which they multiply and cause fibrin formation, leukocytic emigration, degeneration, and coagulation necrosis.

When examined microscopically, the diphtheria membrane is usually found to be laminated, the most superficial layer consisting of fibrin and epithelial cells in a state of coagulation necrosis, beneath which are fibrin networks with leukocytes, etc.

The diphtheria bacilli are present in immense numbers, but only at or near the surface. They do not descend into the deep tissues. The bacilli do not, as a rule, enter the circulation, though in fatal cases of the disease it is not unusual to find a few bacilli in the heart's blood.

There is a loose attachment of the membrane to the denuded areolar tissue by a coarse fibrin network. The connective tissue is somewhat hyperemic, and is infiltrated with leukocytes, some of which contain diphtheria bacilli: there may be some masses of fibrin in the deeper tissues, but the disease is essentially a superficial inflammation.

The lymphatic glands of the neck and the tonsils are usually enlarged, and in the lymph-nodes of the tonsils one can occasionally recognize the fibrin network.

In cases which recover the membrane sometimes detaches in its entirety, especially in cases in which antitoxin has been used. This leaves a denuded surface upon which the epithelium soon forms, but which remains hyperemic for months after. When the membrane does not exfoliate, it disappears by gradual absorption, becoming shredded, fenestrated, thinned, and gradually eroded. In these cases recovery is slower than where the entire membrane is exfoliated.

Diphtheria, however, is not only a local affection of the throat, but also a dangerous toxic disease. In the local lesion the diphtheria bacilli form toxin which is absorbed and distributed. Oertel was the first to devote much attention to the histologic changes produced in the organs by the toxin, and since his observations much work has been done upon the subject. The disseminated toxin has a marked destructive effect upon the tissues, manifested by the formation of numerous minute foci in which the cells are destroyed and their nuclei fragmented, the chromatin being scattered about in granular form. Such foci are found in the tissues in extreme cases of human diphtheria, but can be most conveniently studied in animals that succumb to large doses of diphtheria toxin.

It may be that death from diphtheria intoxication depends in part upon the occurrence of these focal lesions. The severity of the intoxication bears no relation to the extent of the throat lesion, but depends entirely upon the virulence of the particular bacillus. A virulent bacillus sometimes causes fatal intoxication from a very circumscribed and limited lesion, while a membrane that fills the entire pharynx may be caused by bacilli of such feeble virulence that the patient is scarcely made ill by the quantity of toxin generated.

The intoxication sometimes causes sudden cardiac palsy, but the paralysis most frequently seen in diphtheria appears during convalescence. It may occur after any case of diphtheria, but usually follows severe cases. It most commonly affects the muscles of the throat, especially the levatores palati, and interferes with deglutition. It also frequently affects the muscles of accommodation. Monoplegia, hemiplegia, and paraplegia may occur. The nervous lesions are peripheral neuritis. The central lesions consist of toxic irritation, with atrophy or degeneration of the ganglionic cells.

In the streptococcous pseudomembranous pharyngitis the disease is more local, but possesses a danger from which diphtheria is nearly free. The streptococci penetrate deeply into the tissue, and not only provoke more violent local symptoms, but are constantly in danger of transportation to remote parts, where secondary abscesses may form.

Secondary abscesses in diphtheria usually depend upon accidentally present streptococci and not upon the dissemination of the diphtheria bacilli.

Phlegmonous pharyngitis with abscess formation usually follows diphtheria or scarlatina, and depends upon the accidental entrance of the pyogenic cocci into the deep tissues of the pharynx. It is occasionally brought about by traumatism, but in such cases, as well as those that follow tuberculous and syphilitic ulcerations of the pharynx, is also probably due to pus-cocci accidentally introduced. Caries of the spinal column may also cause pharyngeal abscess.

Syphilitic pharyngitis is not uncommon. The pharynx is hyperemic, and sometimes has a coating of white mucus. Erosions and ulcerations with fissures are often seen. The *opaline plaques*—slightly elevated, circumscribed, flat, reddish or bluish-white prominences, which later take on a pearl-like appearance, are occasionally found, and seem to be characteristic. It may be stated, however, that though sore throat is a very common symptom of syphilis upon which much diagnostic importance is to be placed, it is a difficult matter to make a diagnosis from the appearance of the throat alone.

Tuberculosis of the pharynx is not common. The lesions consist of sparsely distributed small tubercles upon a hyperemic surface. The tubercles ultimately soften, and leave ulcers that may continue to increase in size until, in extreme cases, nearly the entire pharyngeal mucous membrane is destroyed and transformed into an uneven ulcerated surface.

Tuberculosis of the pharynx nearly always accompanies or succeeds tuberculosis of the lungs. It is practically unknown as a primary disease.

The tumors of the pharynx are not numerous. Occasional teratoid tumors—hairy polypi, etc.—are seen. Most of the pharyngeal tumors develop from the connective tissues. Birch-Hirschfeld has seen *fibroma*, *fibrosarcoma*, *round-cell sarcoma*, *myxoma*, *plexiform myxosarcoma*. Carcinoma is occasionally but rarely seen. It usually extends by continuity of tissue from contiguous tissues, and causes early extension to the lymphatic glands and leads to early death. The most common form is squamous epithelioma.

THE SALIVARY GLANDS.

The diseases of these organs are not numerous, and are for the most part simple in origin and course.

Acute Parotitis.—The parotid gland, the largest of the group, is most frequently affected.

The acute inflammation may be due to traumatism, but in the great majority of cases is infectious. Two principal forms of acute parotitis are recognized, the simple and the epidemic.

Simple parotitis, simple in the sense that it is not epidemic or contagious, is in the majority of cases caused by the accidental entrance of pyogenic bacteria from the mouth into the salivary ducts. The condition is not infrequently suppurative and may cause disorganization of the gland. It is not infrequent as a complication of typhoid, cholera, diphtheria, and other conditions in which the conditions for infection are particularly good.

Epidemic parotitis or **"mumps"** is chiefly a disease of childhood. It is characterized by an inflammatory enlargement of the parotid gland of one or both sides. The organ swells to a marked degree from serous exudation, and is tense and painful. All the indications are that suppuration is imminent, yet this stage of the inflammatory process is rarely reached, and after a few days the exudation is absorbed and the patient recovers. It occasionally happens that as the disease recovers at the original seat it unexpectedly reëstablishes itself in the testicle and ovary, where the same painful swelling occurs.

The etiology of the affection is obscure, but a number of workers have found that by catheterization of the parotid duct it was possible to secure and cultivate a small diplococcus, first described by Laveran. The disease is highly contagious and not infrequently epidemic.

Both forms of inflammation less frequently attack the submaxillary and very rarely the sublingual gland.

Angina Ludovici.—The infections that occur in the neighborhood of the submaxillary glands are not always confined to the glands themselves, but may rapidly extend to the surrounding cellular tissue, with resulting phlegmonous and even gangrenous changes. Such cases are described as angina Ludovici, or Ludwig's angina, and can scarcely be regarded as a disease of the salivary glands, but rather as a form of cervical cellulitis.

Ludwig's angina sometimes succeeds scarlatina. It is also known to occur from infection of the soft parts by carious teeth, etc. The abscesses usually evacuate externally, but may rupture into the mouth. The gangrenous cases are often fatal.

From any of the simple inflammations or from traumatism, subacute and chronic changes characterized by connective-tissue induration in the glands may take place. In their course, atrophy of the glands and stenosis of their ducts may occur.

Salivary fistulæ, or communications between the mouth and exterior, between the mouth of the duct and the gland, are rather rare results of traumatism or such diseased conditions as suppuration, etc., in which there is local loss of tissue.

Salivary cysts are not infrequent. They are almost without exception retention cysts, caused by the dilatation of ducts whose outlet is constricted or closed. The most frequent and classic is the form known as *ranula*. This, when typical, is a cyst, which occurs from dilatation of the Blandin-Nuhn's glands, small acinous glands situated near the tip on the under side of the tongue. The name is, however, also applied to retention cysts of the sublingual gland, and, indeed, to most other cysts of that vicinity.

Salivary cysts often attain the size of a walnut. Occasionally they are spoken of as *sialoceles*.

Salivary calculi or **sialoliths** are occasionally found in the cystic dilatations of the salivary glands. They usually form about foreign bodies which have accidentally entered the ducts.

The stones consist chiefly of phosphate and carbonate of calcium, and at times of inspissated saliva. They are usually of an elongate form, corresponding to the shape of the duct in which they are formed, and may be branched. Their size is sometimes considerable, Richter having seen one that weighed 34 grams, and Hulke one that weighed 67 grams. The latter had for its nucleus a minute splinter of wood.

Tumors are common in the salivary glands, the greater number being simple connective-tissue tumors. Fibroma, myxoma, chondroma, and sarcoma are not infrequent. They all form encapsulated, more or less rounded growths. As the sarcomata grow large there is a tendency to spread. Those of rapid growth are more malignant than others, and the usual rules as to the determination of malignancy apply.

The epithelial tumors are more rare. Adenoma is occasionally seen. Carcinoma usually develops from a focal point and invades the gland.

The most frequent tumor of the parotid gland is that well known as the *mixed tumor*. It is composed of cartilaginous, mucous, and fibrous tissue, with many of the characteristics of sarcoma. The tumors often appear in childhood and grow slowly until they attain considerable size. In spite of their sarcomatous appearance, they are usually benign in disposition and when excised, seldom recur.

Many of the tumors present beautiful hyaline formations, such as characterize cylindroma.

The tumor probably has its origin in remnants of fetal fragments which, in the development of the cheeks, become included in the parotid structure. Such mixed tumors are found only in the parotid gland.

Parasites are not common in the salivary glands. Salzer has observed the echinococcus in one case.

Syphilis rarely affects the salivary glands. Gumma has, however, been observed.

Tuberculosis of the salivary glands is extremely rare.

THE ESOPHAGUS.

Malformations of the esophagus are not infrequent. The tube may end abruptly in a blind extremity at its upper third, and begin again a little lower down, at a communication between the esophagus and trachea.

Fistulous communications with the trachea are of rare occurrence and are found at varying heights. Fistulæ may also occur in the sides of the neck and pharynx. In some cases the esophagus is double. In rare cases with marked deformity of the body the esophagus may be absent. This condition, however, is usually seen in acardiac monsters.

Stenosis, or marked narrowing of the esophagus, may be caused by intrinsic and extrinsic conditions. It occurs either at the pharyngo-esophageal junction or at the cardiac extremity.

Extrinsic Causes.—*Compression* is seen in cases of enlargement of the thyroid gland, tumors, aneurysms, and other lesions which press upon the gullet and obstruct it.

Obstruction from the lodgment of foreign bodies—jack-stones, false teeth, etc.—which have been swallowed but failed to pass down as far as the stomach is not infrequent. Obstruction also occasionally results from varicosities of the submucous veins in obstructive heart disease and other venous obstructions, and is said by Ziegler occasionally to depend upon mycosis, as in the rare cases in which the Oïdium albicans has established itself in the esophagus. Any tumor growth within the esophagus may become a cause of obstructive stenosis.

Strictures are the most frequent sources of esophagus obstruction. They may be the result of cicatricial formations following the deglutition of caustic substances, such as ammonium, carbolic acid, mineral acids, etc.

Syphilis of the esophagus is rare, but is likely to be followed by stenosis.

Cancer of the esophagus, by projecting into its lumen or by transforming its elastic walls into dense inelastic tissue, is also a cause of marked stenosis.

The stenoses of the esophagus are very frequently followed by secondary dilatation of the higher portion of the tube, thus giving rise to ectasis—esophagectasis—or dilatation.

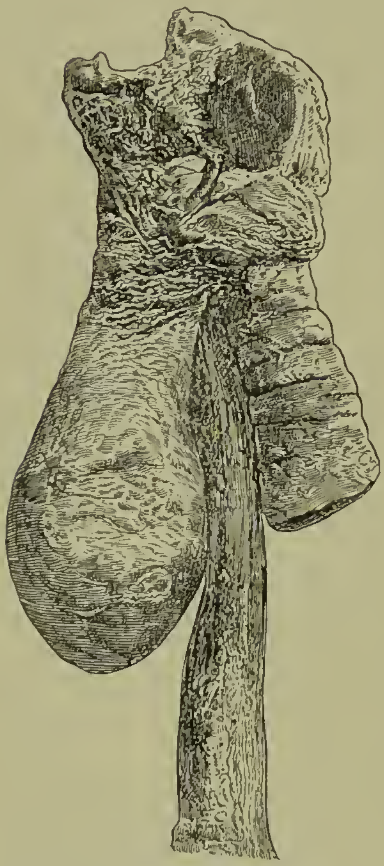

FIG. 250.—Large pulsion diverticulum of the esophagus. Lateral view (after Zenker).

Dilatation of the Esophagus.—Dilatation of the esophagus is the natural outcome of obstruction. Food being swallowed, it enters the gullet, descends to the seat of obstruction, and then, failing to pass and enter the stomach, remains and distends the tube. Any stenosis may, if it diminish the caliber of the tube sufficiently, cause dilatation.

The dilatations usually affect the entire circumference of the tube, though at times the distention may be greater on one side than upon the other.

In rare cases dilatations occur without stenosis, and the esophagus presents the appearance of a pouch, largest at its center. Exactly why such a change should take place is doubtful. Some refer it to muscular contractions at the cardiac end of the tube, others to loss of the muscular elasticity of the esophageal walls. The walls of the esophagus are almost always thickened, the chief hyperplasia occurring in the muscular coat. Rarely small ulcerations occur in the mucous membrane near the gastric termination.

In rare cases dilatation of the lower part of the esophagus is congenital, and a pouch is formed which corresponds to the first stomach of ruminants.

Diverticula of the Esophagus.—Diverticula are local expansions of the esophageal walls with the formation of cecal pouches communicating with the tube by a more or less constricted mouth. Their formation may depend upon the action of internal conditions which force the wall of the esophagus outward, or upon external causes which make traction upon it. Two classes are described by von Zenker:

I. Pulsion or pressure diverticula.
II. Traction diverticula.

I. **Pulsion or pressure diverticula** occur chiefly in that part of the tube which experiences the greatest pressure from the swallowed food. This point is probably at or near the pharyngo-esophageal junction, where, in fact, most of the pouchings occur. They may project posteriorly or laterally, and usually are rounded sacs, varying in size from a pea to a hazelnut. They may, however, attain the size of a pear and form pendulous pouches filled with food that has entered during deglutition. The coats of the esophagus may all be present, or it may be that the muscularis is absent and the pouch is formed by the projection of the mucous and submucous coats through it.

The food that enters the diverticulum is retained for some time and undergoes putrefactive changes which not infrequently lead to inflammatory changes in the mucous membrane of the diverticulum itself and in the adjacent mucous membrane of the esophagus. This inflammatory reaction causes thickening of the walls of the sac, with occasional papillary outgrowths.

The formation of the diverticulum probably finds its predisposing cause in injuries of the esophagus such as result from ulcerations and the presence of foreign bodies. The lateral diverticula may also follow developmental defects in the closing of the bronchial arches and imperfections of the cervical tissues and organs.

II. **Traction diverticula** are more frequent and originate in the traction exerted upon the esophageal wall by adherent, enlarged lymphatic glands and by inflammatory bands attached to other organs and tissues. They form pouches projecting anteriorly, and differ from the pulsion diverticula in being more like a funnel than like a bag in shape. The walls may be perfect, or the muscular coat may be missing and the chief components be mucosa and submucosa. At the apex of the funnel the tractile band is found. There is usually much disturbance of the neighboring tissues, and the esophagus, the trachea, the bronchial lymphatic glands, and other structures are firmly adherent to one another.

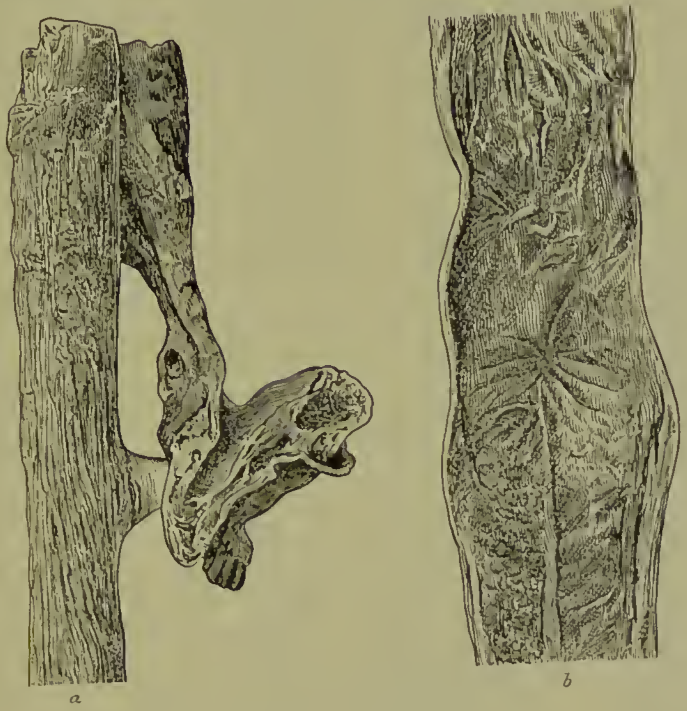

FIG. 251.—*a*, Traction diverticulum of the esophagus (lateral view); *b*, traction diverticulum of another esophagus (internal view) (after Zenker).

The tendency for progressive increase in size which characterizes the pulsion diverticula is absent here, as the force propelling the food has nothing to do with the diverticulum formation. Perforation occasionally happens through laceration of the apex of the diverticulum should the tension become too great.

Rupture of the esophagus may occur in healthy gullets as the result of traumatism, but is very rare. A few cases are recorded in which the tube has been ruptured during violent efforts at vomiting. Such lacerations may be longitudinal or transverse. Ziegler is of the opinion that such lacerations are made possible by changes wrought in the esophageal tissues by frequently regurgitated digestive juices from the stomach. The partial digestion leads to softening of the tissue—*esophagomalacia*.

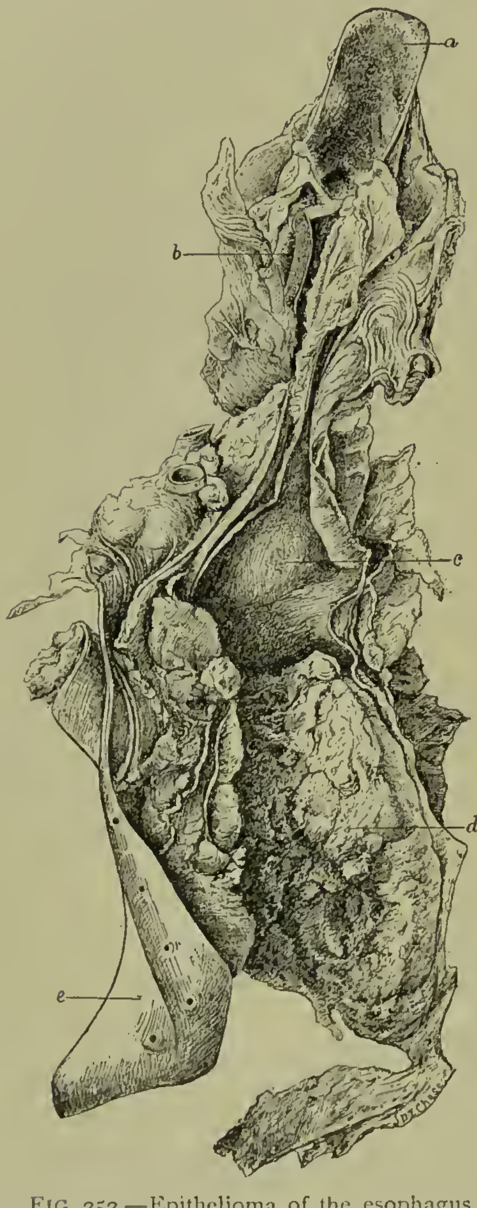

FIG. 252.—Epithelioma of the esophagus: *a*, Epiglottis; *b*, larynx; *c*, dilated esophagus with the posterior wall pressed forward by enlarged lymph-glands; *d*, enormous degenerating tumor-mass through which a very small channel permitted food to enter the stomach; *e*, aorta.

Perforation of the esophagus may depend upon internal and external causes. The most frequent internal causes are simple, syphilitic, or cancerous ulcerations which destroy the tissues, weaken the wall of the tube, and cause it to yield before the distending force of the descending food. Occasionally in bed-ridden and marasmatic patients necrosis of the esophageal tissues is brought about by the pressure of the cricoid cartilage, and may be succeeded by perforation.

The external perforations may depend upon suppuration, caseating tuberculous glands, gummata, aneurysms of the aorta, etc., which gradually embrace or erode the esophageal walls until they finally give way.

Perforations are probably always succeeded by the infection of the lacerated tissues and the establishment of inflammations, which may be mild or may become phlegmonous or gangrenous.

Carcinoma of the esophagus frequently leads to perforation. The opening sometimes leads into a bronchus, and the subsequent passage of food through it and its inspiration into the deeper parts of the lung may lead to purulent bronchitis, or, as I have seen, to gangrene of the lung.

Inflammation of the esophagus (esophagitis) may be caused by the injurious action of foreign bodies, by irritating or injurious substances swallowed, or by infection.

1. **Catarrhal Inflammation of the Esophagus.**—The morbid anatomy is very simple, consisting of congestion, infiltration, and thickening of the mucous and submucous coats, and desquamation of the epithelium. The inflamed esophagus is nearly red. Ulcerations are occasionally seen. This form of inflammation may be general or may be local if caused by a foreign

body. If the inflammation becomes chronic, the coats of the tube are thickened and thrown into folds. Polypoid projections from the surface of the mucous membrane and cysts formed by obstruction of the mucous glands are common. Chronic esophagitis is almost invariable in drunkards.

2. **Croupous inflammation** usually depends upon infection with the streptococcus (?). True diphtheria of the esophagus is quite rare. Croupous or pseudomembranous esophagitis is occasionally met with in typhoid fever, scarlatina, measles, variola, cholera, phthisis pulmonalis, and similar affections. The ordinary characteristics of the pseudomembranous inflammations are observed. When corrosive substances have been swallowed, the surface of the esophagus is sometimes covered with a pseudomembrane formed from the destroyed superficial tissue.

3. **Phlegmonous esophagitis** results from the rupture of abscesses into the esophageal walls and from perforations. A curious but rare effect of extensive abscess formation in the wall of the esophagus is the occurrence of permanent cavities or spaces beneath the mucosa, which has been elevated by the pus. After rupture and evacuation, instead of collapse and organization, these cavities become lined by epithelium and persist.

4. **Mycotic esophagitis** caused by Oïdium albicans occurs in rare cases of thrush.

Syphilis and tuberculosis rarely attack the esophageal tissues. When the latter occurs, it is usually by extension of the disease to the esophagus from neighboring tuberculous lymphatic glands.

Tumors of the esophagus are not common. The ordinary connective-tissue tumors—fibroma, myxoma, myoma, lipoma, etc.—are occasionally observed. They are usually polypoid in form. Sarcoma and papilloma (verrucæ esophagi) are more rare.

The most frequent neoplasm of the esophagus is the **squamous epithelioma.** It may occur at any part of the organ, but is most frequent at the lower third, where the organ is crossed by the left bronchus. It forms a flat, tabular swelling, the center of which soon becomes ulcerated. As the ulcer spreads, the tumor is recognizable as an extensive ulceration surrounded by a dense, hard, cicatricial connective-tissue border. Beginning in the mucosa, the submucosa and muscularis are successively invaded, and ultimately the surrounding tissues may be infiltrated. The disease leads to marked stenosis, which is naturally followed by dilatation, this by retention of food and infection of the ulcerated tissues. The disease may extend to the neighboring lymphatic glands, trachea, bronchi, pericardium, pleura, lungs, and heart. Perforation of the esophagus not infrequently follows the epitheliomatous ulceration and stenosis.

Cancer of the esophagus is much more frequent in men than in women, and is especially frequent in drunkards.

DISEASES OF THE STOMACH.

Congenital Anomalies.—Complete absence of the stomach is a rare condition, usually seen only in acardiac monsters. The stomach is occasionally abnormally small. Rarely it is without its normal outlet into the duodenum, and connects with the intestine only by a fibrous cord. Sometimes the organ is double, in the sense of consisting of two pouches separated from each other by a marked intermediate constriction, and is then spoken of as an "*hour-glass stomach.*" Such organs sometimes result from the cicatrization and subsequent contraction that follow the healing of large ulcerations. In cases of transposition of the viscera the position of the stomach is reversed.

Circulatory Disturbances.—Anemia of the mucous membrane of the stomach occurs as a part of general anemia. In this condition the mucosa is pale and may be thinned. The normal rugæ are often lost, and the surface of the organ appears unusually smooth. The stomach is sometimes much smaller than normal, particularly in cases of pernicious anemia. It is thought by some, however, that the atrophy of the stomach is the cause, and not the effect, of the anemia.

Hyperemia.—Functional hyperemia causes a delicate rosy hue of the mucous membrane during digestion. Acute congestion of the stomach depending upon the presence of irritating substances is characterized by a more intense color and by irregular distribution in streaks and patches corresponding to the parts chiefly acted upon by the irritant. The apical portions of the larger rugæ of the pyloric extremity most frequently show the red color.

Passive hyperemia of the stomach follows venous stasis in heart disease and cirrhotic hepatitis. The mucous membrane is not red, as in the acute hyperemia, but appears purplish in color. When the congestion is of protracted duration, the submucosa may appear edematous. The blood frequently extravasates from the veins, and small interstitial hemorrhages are common. The fresh hemorrhages have the usual dark color, while old hemorrhages appear as brownish or yellowish spots.

Hemorrhages.—Hemorrhages into the mucous membrane of the stomach occur with great frequency. Indeed, Birch-Hirschfeld states that careful examination will reveal their presence in about one-half of the cadavers examined. He looks upon the majority as caused by pre-agonal vomiting. They usually appear as punctiform or linear, submucous, purplish or reddish-brown discolorations. Not infrequently the hemorrhagic area is not properly protected from the gastric juice by alkaline mucus, so that if they have occurred some time before death, the mucous membrane is eroded. This condition is described as *hemorrhagic erosion* of the stomach.

Punctiform hemorrhages are also seen in the infectious diseases, such as typhoid, purpura, etc., and in acute atrophy of the liver, as well as in the chronic congestions following cirrhosis of the liver and cardiac disease.

Massive hemorrhages from the stomach—*hematemesis*—are seen in peptic ulcer (*q. v.*) and in carcinoma, and sometimes from traumatism caused by swallowing foreign bodies.

In *peptic ulcer* the hemorrhage results from the erosion of a blood vessel, and may be fatal if the eroded vessel be large enough to permit of so extreme a loss of blood. In the *traumatic lesions* the extent of the hemorrhage corresponds to the extent of the injury done the gastric membrane. In both conditions the vomited blood may appear bright red and arterial in appearance, or, if retained for some time in the stomach, may be altered by the action of the gastric juice and resemble coffee-grounds.

In *cancer of the stomach* with considerable ulceration hemorrhage is chiefly due to oozing from the capillaries. The blood escaping is slowly altered by the gastric juice, and rarely appears normal, the "coffee-ground vomit" being quite typical.

A peculiar hemorrhagic condition of the stomach and duodenum of newly born infants is called *melæna neonatorum*, and is accompanied by the formation of ulcers in the mucous membrane. Some think that it depends upon cerebral lesions, but there is as yet no definite information upon the subject. Schiff and Ebstein have carefully studied the effect of brain lesions upon the vascular condition of the stomach, and found that in 23 experimental punctures of the corpora quadrigemina, etc., gastric hemorrhage resulted in 9.

Bleeding from the stomach also occurs in *hemophilia* and in rare cases of *vicarious menstruation*.

Thrombosis of the gastric vessels is uncommon. It is supposed to be a cause of peptic ulceration. It sometimes occurs after extensive burns of the surface of the body, and is followed by the sudden formation of ulcers of the pylorus and duodenum which progress to rapid perforation from subsequent erosion by the digestive juices.

Embolism of the gastric vessels is not uncommon in cardiac disease. There is such free anastomosis of the gastric vessels, however, that, except the embolus be infectious, it is unaccompanied by important changes. Infectious emboli lead to the formation of abscesses and ulcers of the mucous membrane.

Effect of Gastric Juice upon the Stomach.—The gastric juice is without effect upon the walls of the stomach during health. Exactly what protects the mucous membrane is not known. Hunter believed that "the principle of life" keeps living things from being digested. Bernard believed that the epithelium of the stomach acted as a protective to the organ, preventing the absorption of the gastric juice. Others think that the mucus formed by the gastric mucous membrane, being alkaline, acts as a protective coating; still others that the alkaline blood circulating in the mucosa neutralizes the acid of the gastric juice and thus prevents the possibility of peptic digestion.

As Howell points out, the question is more complicated than at first appears, for unicellular organisms prepare digestive juices which will digest incorporated bodies without digesting themselves, and thus shows us that the protective power is probably "a peculiarity of structure." "When it is said that the exemption of living tissues from self-digestion is due to peculiarities of their structure, it must not be supposed that this is equivalent to referring the whole matter to the action of a mysterious vital force. On the contrary, all that is meant is that the structure of the living protoplasmic material is such that the action of the digestive secretion is prevented, possibly because it is not absorbed, this result being the outcome of the physical and chemical forces exhibited by matter with this peculiar structure."

Upon abnormal tissue, however, the case is quite different, and the gastric juice readily dissolves it, forming the "peptic ulcer."

Peptic Ulcer.—A peptic ulcer is an erosion caused by the action of the gastric juice upon diseased tissue.

Etiology.—The exciting cause is the proteolytic action of the gastric juice. The most frequent predisposing causes are probably the small hemorrhages of the mucosa already mentioned.

Infection, embolism, and thrombosis of the gastric vessels from ischemia following arteriosclerosis, spasms of the blood vessels, etc., are factors of importance. General anemia, especially in chlorosis, seems to predispose to ulceration. Increased acidity of the gastric juice, whether the result of therapeusis or disease, by increasing its activity, favors ulceration. It has also been shown experimentally by Somnelsohn that the alkalinity of the blood has much to do with the protection of the gastric mucosa, for when the acidity of the gastric contents was increased to 2 per cent., it did not affect the normal mucosa, even when the alkalinity of the blood was destroyed. When, however, the gastric contents were artificially increased to 5 per cent. and the alkalinity of the blood destroyed, the gastric juice at once attacked the mucous membrane.

Morbid Anatomy.—Morbid growths of the stomach are usually more or less corroded, but as in these cases the gastric juice loses its acidity, alterations in structure that would ordinarily predispose to erosion escape it. The lesions appear as larger or smaller, more or less rounded, losses of substance. They may be confined to the mucosa, may involve the submucous layer, include the muscularis, or even in some cases destroy the serous coat. According to the classic description, the peptic ulcer appears as if cut out with a punch. It is, as a rule, crater-like, being wider at the top than at the bottom, and when several coats are involved, is distinctly terraced, the lost tissue in each coat being of less extent than in the more superficial layers. The true peptic ulcer is accompanied by very little inflammation.

The ulcers are usually single, though Osler mentions a case in which 34 were present. The size is usually small, varying from 1 to 4 cm. Peabody has seen one which measured 10 by 19 cm.

Gastric ulcers do not always produce clinical symptoms, as they are much more frequently discovered at autopsy than would be expected. In 2330 autopsies at Prague reviewed by von Jaksch, peptic ulcers occurred in 113 (5 per cent.). In 13,665 autopsies reviewed by Leube, there were 623 ulcers or healed scars—5 per cent. Of 1699 cases which Welch has collected, 40 per cent. were males and 60 per cent. females, so that it is much more frequent among females than among males.

The ulcers are generally situated upon the posterior wall of the stomach, at or near the lesser curvature, and are much more frequent near the pyloric than toward the cardiac end.

Peptic ulcer may also occur in the duodenum, but less frequently than in the stomach. Men more frequently suffer from duodenal ulcer; women more often from gastric ulcer.

The termination of the ulceration is interesting. Most commonly it heals kindly. The corrosion progresses until all the devitalized or diseased tissue is digested, then, as the gastric juice begins to act upon the healthy tissue, a reactive inflammation begins at the periphery, cicatrization occurs, followed by contraction, until only a rounded, more or less radiating scar is formed. Large ulcerations probably last a long time before regeneration occurs. Hour-glass stomach is formed by the contraction following large scars.

There is no new formation of muscular tissue in the scar. The mucosa, however, regenerates perfectly and is provided with normal glandular tissue.

The scar is easily recognized by its white color and stellate shape.

Small simple and otherwise unimportant ulcerations may erode blood-vessels and cause hemorrhage that may prove fatal. The vessels most frequently eroded are the splenic artery and the artery of the lesser curvature or their branches.

Deep ulcers may perforate and permit the escape of the gastric contents into the peritoneum with resulting peritonitis. Fortunately, this is commonly prevented by the position of the ulcerations, which make possible inflammatory adhesions between the stomach and liver, stomach and pancreas, stomach and diaphragm, and stomach and spleen. Even when they occur anteriorly, it is possible for adhesions to form between the stomach and colon and prevent the contents of the stomach escaping into the peritoneal cavity. Fistulous communications may be established between the stomach and the transverse colon and between the stomach and duodenum. Ruptures through the diaphragm into the pericardium have been seen, and Osler speaks of cases that finally ruptured into the left ventricle of the heart. Rupture of the diaphragm into the pleura has also been seen.

When the stomach unites with the liver or pancreas, fibroid changes occur in the respective organs near the seat of union. Infection occurs, and abscesses usually form.

The most unfavorable ulcerations are situated on the anterior aspect of the stomach, where adhesions can be formed with difficulty. These cases are apt to rupture into the peritoneal cavity. Some ulcers of the posterior wall rupture into the lesser peritoneal cavity. They may lead to the formation of subphrenic abscesses, and also at times to fetid purulent inflammation between the liver and diaphragm. Sometimes such cases give rise to gaseous distention extruding upward into the thorax, and described as subphrenic pyopneumothorax.

Gastromalacia is a softened condition of the walls of the stomach commonly seen at autopsy, and without doubt resulting from the postmortem action of gastric juice upon its tissue. In cases of slow death in which there is a profound alteration in the circulation of the stomach, it may be possible for the conidtion to occur during the death agony, but, as ordinarily seen, the process is without doubt the result of the combined maceration and digestion of the dead tissue. The condition is most marked in cases of hyperacidity or in those dying during digestion. It is common in infants, probably because of lactic-acid fermentation in the stomach.

It is first observed in that portion of the stomach in actual contact with the contents, and a line of circumscription may be observed corresponding to the fluid level. The result of the digestion and maceration is so marked a softening of the tissue that it may rupture spontaneously and allow the escape of the contents of the stomach into the peritoneum. The post-mortem nature of this change can be determined by noting the absence of peritonitis.

This appearance of the stomach should be learned early, so that it may not be confounded with pathologic conditions.

If the mucous membrane be anemic and the contents of the stomach free from discoloring substances, the gastromalacic wall appears pale gray in color and has a gelatinous consistence. This is spoken of as *gelatinous softening*, and is most frequently seen in infants.

When the mucosa is congested at the time of death and there is considerable blood in the veins, the transformation of the hemoglobin into hematin causes the tissues to take on a more or less intense, reddish-brown color, which is much intensified along the lines of its veins. The final stage is the transformation of the tissues into a mushy, non-resisting mass. This is described as *pulpy* or *brown softening*.

INFLAMMATION OF THE STOMACH.

Acute gastritis usually depends upon internal causes, the most common being irritants, such as alcohol, indigestible foods, etc. Some cases may depend upon infection. A smaller number of cases result from the extension to the stomach of inflammations of neighboring organs.

The pathologic anatomy is extremely simple. There is a more or less marked hyperemia of the mucosa, which appears red, somewhat thickened, and covered with an unusual amount of mucous secretion. There may be occasional small submucous hemorrhages.

Microscopically, the wall of the stomach is but slightly changed in structure. The mucosa is thickened and congested, and the epithelial cells of the glands and of the surface are in a condition of cloudy swelling. An enormous number of goblet cells are present. The cloudy swelling makes it impossible to distinguish between the chief and parietal cells of the glands. Many of the cells desquamate, remaining in the characteristic coating of tenacious mucus. The disease is essentially catarrhal in character. The areolar tissue about the glands is infiltrated with leukocytes.

Pseudomembranous gastritis occasionally results from the action of swallowed caustic substances, or from certain of the specific infectious diseases, such as scarlatina and small-pox. It also occasionally results from true diphtheria. In all forms the characteristic feature is the occurrence of grayish-white pseudomembrane which forms in smaller or larger patches, or upon extensive surfaces of reddened and inflamed mucous membrane. In true diphtheria the necrotic process may extend so deeply that the entire mucosa is transformed into part of the false membrane.

Mycotic Gastritis.—Parrot has seen a few cases in which *thrush* has become a widely distributed disease with patches in the stomach.

Phlegmonous gastritis is a very rare disease, caused by the streptococcus and characterized by the formation of more or less circumscribed abscesses. The neighboring tissues are affected by contiguity and become infiltrated with pus. The abscesses ultimately rupture into the cavity of the stomach. If the patient does not die, recovery is not always by cicatrization with contraction, but by growth of the epithelium from the neighboring mucosa into the cavity. If there were numerous apertures, there will be a corresponding number of communications between the interior of the stomach and the submucous cavity.

Chronic gastritis may result from repeated acute attacks, or may be chronic from the beginning. It is a common result of the abuse of alcohol, of habitual indulgence in indigestible foods, the excessive use of tobacco, and insufficient mastication. It also results from certain constitutional disorders, such as anemia, gout, tuberculosis, diabetes, and Bright's disease, and may occur from purely local conditions, such as cancer of the stomach, chronic congestion of the stomach from cirrhosis of the liver, chronic heart disease, etc.

Simple Chronic Gastritis.—In this form of the affection one not infrequently sees indications of the primary acute disease, in the form of hemorrhagic erosions, more or less marked ulcerations, loss of mucous membrane where pseudomembranes have been attached, cellular infiltration of the mucosa, hyperplasia of the submucosa, etc. The stomach is usually capacious, though it may be smaller than normal. The mucosa is usually thickened from infiltration and hyperplasia. The proliferated connective tissue is irregularly distributed in the submucosa, and not infrequently circumscribes islands of normal mucosa which project above the surface. A marked wrinkling of the mucous membrane near the pylorus, accompanied by the presence of numerous nodular and polypoid projections, give it the name *polyposis ventriculi.* The French pathologists speak of this condition as an "*etat mammelone.*"

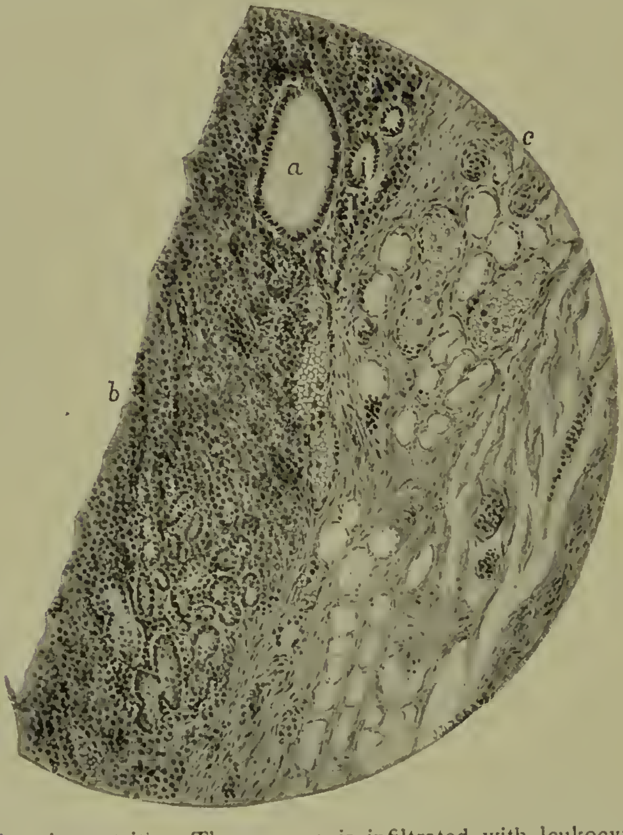

FIG. 253.—Chronic gastritis. The mucosa is infiltrated with leukocytes, the glandular tissue has in part disappeared, and some of the glands (*a*) have developed into cysts; *b*, mucosa; *c*, submucosa.

Sclerotic gastritis is a chronic interstitial form of the disease. It may have its origin in prolonged mild irritation or in peculiar systemic intoxication in profound anemia or in systemic depression.

It is characterized primarily by increase in the fibroconnective tissue of the wall of the stomach, secondarily by its contraction, which destroys the glandular tissue. Partly destroyed glands sometimes have occluded outlets and dilate into cysts.

The mucosa may be so thinned as to be only one-half or one-third its normal thickness, but the connective tissue is, nevertheless, increased and contracted so as to form an actual *atrophic induration*. Upon the atrophic surfaces one occasionally finds large, indefinitely outlined ulcerations. The stomach may be enlarged—dilated. Some speak of the condition as *phthisis ventriculi*.

In other cases the connective-tissue proliferates to a much more marked extent, and contracts so uniformly as to reduce the capacity of the stomach to a few ounces. The walls of the stomach may be unusually thick and the mucosa wrinkled. The chief increase is in the connective tissue of the submucosa, but the muscular tissue may also be increased. The loss of glandular tissue is less apparent than might be expected because of the diminished surface over which it is distributed.

This form of chronic gastritis is sometimes called *cirrhosis ventriculi*.

In both conditions it is common to observe small interstitial hemorrhages, small round-cell infiltrations, and a grayish or slate-colored discoloration caused by clusters of pigment-granules in the mucosa. Ziegler also speaks of the presence of peculiar hyaline granules in the tissue.

The epithelial cells of the atrophic mucosa are lost, in part by desquamation, and in part by degeneration. Goblet cells are very numerous.

The changes of chronic gastritis, and, indeed, of nearly all forms of gastric disease, are most marked in the neighborhood of the pylorus, where marked contraction of the connective tissue may lead to stenosis.

Chronic interstitial gastritis is most frequently seen in drunkards, and is known to German pathologists as "Säufermagen."

Local anemia and tissue necrosis follow contraction of the hyperplastic connective tissue, and are not an infrequent cause of peptic ulcerations. They are not usually serious, but result in cicatrices which further increase the deformity of the organ.

An occasional proliferation of the parietal cells of the gastric glands, together with hyperacidity of the gastric juice and loss of the surface epithelium, has led Hayem to suggest that two different types of chronic gastritis may be separated by the histologic changes in the gastric glands. The condition in which the parietal cells proliferate, the surface epithelium becomes desquamated or destroyed, and the secretions are excessively acid, he describes as *gastritis parenchymatosa hyperpeptica*, while for a form characterized by loss of the parietal cells, proliferation of the chief cells, and diminution of the acid in the secretion, he suggests the name *gastritis parenchymatosa mucosa*. Birch-Hirschfeld points out, however, that the anatomic pictures are not similar, and may result from inanition and causes other than gastritis, and by no means always correspond with Hayem's clinical pictures.

THE CELLULAR DEGENERATION OF THE STOMACH.

Amyloid disease occurs in the muscularis, and to a less marked degree in the mucosa. The mucous membrane appears thickened, dull, and translucent to the naked eye. As usual, the disease first makes its appearance in the walls of the vessels. Some have thought that the epithelial cells of the gastric glands underwent amyloid infiltration, because in their places grains of the amyloid substance are often found. It is, however, more probable that the change occurs only in the connective tissue and that its altered cells, pressing upon the epithelium, cause its atrophy and disappearance.

Fatty metamorphosis of the cells of the gastric glands is a part of the morbid anatomy of some of the severe infections and intoxications. When this condition is present, the mucous membrane has a peculiar yellowish-white color and is duller than usual. When a microscopic examination is made, one finds the fat not only in the cells, but also in the interstices of the connective tissue.

Pigmentation of the wall of the stomach succeeds interstitial hemorrhage, and also occurs in chronic gastritis.

Calcification of the stomach is extremely rare and interesting. It has been observed in cases in which there has been a rapid absorption of lime-salts from the bone after poisoning by mercuric chlorid. Whitish, gritty flakes or patches are observed upon the inner surface of the stomach, and upon microscopic examination granules of calcium carbonate are found in its interstitial tissue.

Hypertrophy of the stomach is probably a common result of its habitual distention. The capacity is increased, and the walls are thickened.

Atrophy of the stomach is seen in sclerotic gastritis following marasmus and pernicious anemia, lead-poisoning, and senility. The most important fact in connection with it is that it is usually accompanied by loss of glands and consequent diminution of the digestive ability. The atrophy accompanying pernicious anemia may be the cause, rather than the result, of the anemia. The stomach is small and pale in color, its walls are thin, and the mucosa is smooth and shiny.

TUMORS OF THE STOMACH.

The connective-tissue tumors of the stomach are rare and comparatively unimportant. Among those described are myoma, lipoma, fibroma. Sarcoma is more rare and seems to grow from the lymphoid deposits in the wall of the stomach. It usually assumes a nodular form. Sometimes it occurs as myosarcoma, and in one such case Korinski discovered unstriped muscle-cells in the secondary sarcomatous deposits in the liver.

Lymphangioma is occasionally seen beneath the peritoneum upon the stomach.

Papilloma and polypi usually result from chronic gastritis and are not tumors in the true sense of the word.

Adenoma of the gastric glands have been observed. In rare cases accessory pancreati or displaced pancreatic fragments are situated beneath the mucosa ventriculi. Considerable attention has been paid to these pancreatic tumors of the stomach by Klob. They closely resemble adenomata.

Cancer of the stomach is a common and important disease.

Etiology.—It usually occurs in advanced life, being most frequent between the fortieth and seventieth years. It is occasionally seen earlier, and a few most extraordinary exceptions have been noted; thus, Wilkinson reported a case of congenital cancer of the stomach, and Cullingworth one in a five-weeks-old infant. It is more common in men than in women, in the relation of about 58 to 42 per cent. (Brinton). Occupation seems to have little to do with its occurrence. Countries differ very widely in the frequency with which it is observed. In Switzerland it is very common, about 1.85 per cent. of all deaths depending upon it. On the other hand, Egypt, Turkey, and some other countries seem to be almost entirely free from it.

The exciting cause is unknown. The disease is markedly hereditary. It sometimes seems to follow chronic gastritis, and is thought occasionally to have its starting-point in peptic ulceration.

The disease is almost always primary, and develops from the epithelium at one or the other orifice of the stomach, much more frequently at the pylorus than at the esophagus. Occasionally the walls intermediate between the extremities are affected, the disease in such cases being situated, as a rule, on the posterior wall of the lesser curvature. Hahn, in his statistics of the Friedrichshain Krankenhaus in Berlin, found the following:

Pylorus	60 cases.
Cardia	40 "
Lesser curvature	27 "
Entire stomach	21 "
Greater curvature	8 "
Anterior wall	7 "
Posterior wall	7 "
	170 cases.

Thirteen hundred cases studied by Welch show the following distribution:

Pylorus	791 cases.
Cardia	104 "
Lesser curvature	148 "
Entire stomach	61 "
Greater curvature	34 "
Anterior wall	30 "
Posterior wall	68 "
Fundus	19 "
Multiple	45 "
	1300 cases.

The pyloric cancer grows from the glands of the pylorus. Indeed, the glands, both peptic and pyloric, are the original seat of disease except in squamous epithelioma at the esophageal opening. Both chief and parietal cells take part in the process, the parietal cells sometimes outnumbering the others.

The appearance of the gastric cancer differs very much in different cases. Sometimes it occurs as a dense, scirrhous induration encircling the pylorus and causing stenosis; sometimes as a universal infiltration of the walls of the stomach, with much thickening, induration, and ulceration. At other times it forms a larger or smaller, fungoid mass, soft and spongy, or entirely changed into colloid jelly. The tumors are usually single, but are occasionally multiple.

1. **Scirrhus.**—The scirrhous cancer of the stomach is usually situated at the pylorus. It takes the form of a thickening of the walls with a degree of induration very noticeable to the fingers, and still more marked when an attempt is made to open the stomach, the tissue creaking under the knife. The interior is either smooth, with occasional inconspicuous irregularities, or unusually rugous and marked by alternating elevated and depressed areas, many of the latter being ulcerated. The tissue is usually pale and dry. The pylorus is markedly stenosed.

When the tissue of the diseased area is examined microscopically, very little epithelial tissue is discovered, the mass being made up essentially of cicatricial tissue. The stomach may be greatly increased in size if there is marked stenosis of the pylorus.

2. **Medullary cancer** is also most frequent at the pylorus, but may occur upon the gastric walls. The tumor forms a fungous mass which may be as large as an egg or even as large as an orange. It is spongy, soft, juicy, vascular, and usually has a smooth surface divided into more or less rounded nodes. The tumor is prone to undergo softening as it outgrows its nutrition, and when the center degenerates and is lost, an excavated mass with a crater-like central ulceration is observed.

Microscopically, this tumor exhibits a relatively great amount of cellular tissue, with comparatively little fibroconnective-tissue stroma. The arrangement of cells in the spaces of the stroma is more or less typical in different cases, but is never so perfect as in adenoma. The cells usually retain their cylindric shape but a short time, and in the rapidly growing part of the tumor become spheroid.

3. **Adenocarcinoma.**—This form is characterized histologically by a marked tendency for the epithelial cells to retain their cylindric form and regular arrangement, so that the sections show proliferation of the glandular elements. As the cells become remote from the primitive focus of development, this arrangement becomes less marked, but it is a striking characteristic of the tumor.

Macroscopically, the tumor has no distinctive features. It has been called "*destructive adenoma*," and is frequently called "*cylindric epithelioma*." Its metastases are fewer and its course is possibly slower than the other forms.

4. **Colloid Cancer.**—This is usually a cylindric-celled cancer, which is strongly characterized by the transformation of its cells into colloid substance. The surface of the tumor may show attached masses of the glue-like substance, but the colloid material is usually dissolved away from the surface by the digestive juices, and is found in larger or smaller cysts in the interior of the tumor-mass. The appearance is typical, and the escape of the gelatinous yellowish material when the tumor is incised makes its nature unmistakable.

5. **Squamous Epithelioma.**—This form of gastric cancer is rare and occurs exclusively at the cardiac end. It has its origin from the squamous epithelium of the esophagus, and may invade the esophagus or entire cardiac end of the stomach. Large peptic ulcerations are very frequent. There are no pyloric obstruction and no consequent dilatation of the stomach.

The gastric cancers grow by distributing their irregular clusters of cells throughout the muscularis mucosæ and submucosa. The muscularis is invaded in most cases, and it not infrequently happens that the serosa is also invaded and presents flat, tabular, cancerous masses. Adhesions form between the stomach and the neighboring structures,—omentum, colon, etc.,—and a direct extension of the growth may take place by continuity of tissue. Upon the serous surface of the stomach one is apt to find lymphatic vessels containing distending plugs of cancer-cells. The lymphatic glands of the lesser curvature and many neighboring lymphatic glands become enlarged and are soon involved in the disease process. More remote glands enlarge and sometimes become invaded. The glands of the thoracic, inguinal, and supraclavicular regions are most frequently affected.

The liver is the seat of secondary growths in about 75 per cent. of the cases. Multiple secondary nodes in the liver are most frequent in ulcerating pyloric cancers. The secondary tumors usually correspond in type with the parent tumor.

The scirrhous are more slowly metastatic than the medullary and colloid forms, but may cause extensive changes through pyloric stenosis. This leads to immense dilatation of the stomach, which may be dislocated and descend so low that its inferior border is in the neighborhood of the pubes (*gastroptosis*). The fermentative and putrefactive changes that take place in such organs are aided by the absence of the hydrochloric acid from the gastric juice (*achlorhydria*) which makes the secretion less antiseptic than normal, so that bacteria are able to grow with facility in the ingested and only partially digested food.

The muscular tissue is much thinned by the distention, and the muscular power so diminished that vomiting, though frequent, is less effectual, and the contents of the stomach are in part retained. The absence of hydrochloric acid from the gastric juice prevents the usual erosion of diseased mucous membrane, though when much lactic acid is produced through fermentation, it may occur.

When scirrhous carcinoma occurs in the body of the stomach, the contraction may bring about a deformity known as *hour-glass stomach.*

The soft cancers, and especially the colloid cancer of the stomach, not infrequently rapidly invade the peritoneum, and form larger or smaller masses which may center in the omentum, which rolls up into a bundle and forms a solid mass of elongate form lying transversely in the abdominal cavity. In colloid cancer it may be covered with jelly or riddled with small colloid cysts, or it may contain large cysts. The spaces between the omental mass and the colon, the stomach, the liver, and other organs may be more or less filled with jelly. The colloid jelly in these cases is beautiful in appearance, being clear, amber-colored, and sufficiently firm to vibrate like calves'-foot jelly.

In cancer of the cardiac end of the stomach the conditions usually seen in gastric cancer are reversed and the organ is smaller than usual, possibly because the food is hurried from the irritated stomach into the intestine through the unaltered pylorus. In cases of universal scirrhus of the gastric wall the contraction may cause the organ to become much smaller than normal.

In the softening, ulceration, and erosion of the tissues in carcinoma ventriculi two accidents of considerable clinical importance are possible. The first is *hemorrhage* from ulcerated vessels, the second, *perforation* with peritonitis.

Tuberculosis of the stomach is rare. The probable explanation is to be found in the acidity of the gastric juice. The disease occurs at the pylorus. Sometimes it forms an ulcerated and indurated ring. The ulcers present the usual irregular appearance and indurated borders. The infection may take place through the direct implantation of ingested bacilli in a diseased organ with alkaline contents, or may result from bacilli deposited as emboli in the capillaries of the gastric wall, or through extension from the peritoneum.

Syphilis of the stomach is also a rare affection. The only certainly recognizable syphilitic lesion is the gumma. It is followed by rupture, ulceration, and the formation of large stellate cicatrices. Syphilitic disease of the gastric vessels—endarteritis, etc.—may be the cause of peptic ulcers. Hemorrhagic erosions, hemorrhagic infiltrations, ulcerations, and gummata occur.

Gastroptosis.—Gastroptosis is dislocation of the stomach, and nearly always succeeds pyloric obstruction and dilatation. The organ is dragged downward to an abnormal position by its size and the weight of its contents, so that instead of occupying the epigastrium, it is found in the umbilical region. The shape is also changed, its inferior border having a much more marked curve than usual, and descending toward the pubic region. Gastroptosis is not infrequently associated with dislocation of the colon (gastroenteroptosis) and sometimes of the liver and spleen.

DISEASES OF THE INTESTINES.

CONGENITAL ANOMALIES OF THE INTESTINES.

Total absence of the intestine is an extremely rare condition seen only in the acardiac or extremely rudimentary monsters.

Incomplete development of the intestine presents several interesting conditions:

1. *Atresia* or closure of the bowel is most frequent at the rectum, where the gut may end so high up that there is no true rectum, or may terminate in a blind pouch, there being no anus. The latter cases are usually called imperforate anus.
2. *Cloaca formation*, in which the bowel joins the uterus, the vagina, or the urethra, forming a common outlet for the digestive, urinary, and reproductive systems, is also a rare abnormality.

3. *Diverticula* are not infrequent. The most common is *Meckel's diverticulum*, which arises from the ileum about a meter above the ileocecal valve. It has a varying length, and not infrequently terminates in a bulbous expansion. Sometimes, instead of an enlargement, the diverticulum terminates in a fibrous cord which extends to the umbilicus. It is possible for this branch of the intestine to continue open to the umbilicus, so that fecal matter escapes from that opening. Indeed, the intestine itself has been known to terminate in such a communication with the umbilicus, there being no connection between it and the colon.

Meckel's diverticulum is a persistent remnant of the embryonal structure known as the *vitelline* or *omphalomesenteric* duct. It formed the original communication between the intestine and the yolk-sac of the embryo.

4. *Cysts.*—Excluded portions of the intestinal tissues go on to an atypical development and may form enterocysts. In certain monsters cysts may be formed by the dilatation of imperforate portions of the intestine.

Transposition of the intestine is occasionally seen, the colon ascending on the left side and descending on the right.

Abnormal course of the large intestine seems to be a common anomaly. The cecum is sometimes unusually long, sometimes unusually short; the vermiform appendix varies in position accordingly. Instead of ascending to the liver and forming the hepatic flexure, the large intestine sometimes diagonally crosses the abdomen from the right iliac fossa to the splenic region, then makes an acute angle, and descends. The most frequent of the abnormalities is a V-shaped curve of the transverse colon, the apex of which sometimes descends to the pubes. The sigmoid is very variable, and the sigmoid flexure may be absent, especially when the cecum is large.

Hernia is an abnormal relation of the intestine, resulting from its entrance into or passage through an abnormal opening in the abdominal wall, through an opening in the mesentery, or through the foramen of Winslow.

DISPLACEMENT OF THE INTESTINE (HERNIA).

By hernia is meant the entrance of the intestines into any abnormal or unusual opening. It is common to speak of *external* and *internal* hernias, the former referring to protrusions of the intestines from the umbilicus, inguinal and femoral canals, obturator foramen, etc., the latter, rarer conditions in which the organ enters or passes through openings in the omentum, mesentery, diaphragm, etc., or through the foramen of Winslow.

The cause of hernia is not clear. It has been thought by some to depend upon abnormal length of the mesentery, which gives the intestine an abnormal freedom of motion; by others that an abnormal distribution of fat in the tissues of the inguinal and femoral regions diminishes their resisting power.

It is certain that many cases depend almost entirely upon abnormal conditions, such as arise, for example, from failure of the inguinal canal to close after the descent of the testicle.

Hernias are classified according to their—(1) Position; (2) contents; (3) condition; (4) origin.

According to their position, the hernias are divided into—

External—Inguinal.
Femoral.
Umbilical.
Obturator.
Ischiatic.
Labial.
Perineal.
Internal—Winslowian.
Mesenteric.
Omental.

Inguinal Hernia.—Inguinal hernia is the descent of some of the abdominal viscera into the inguinal canal. If the hernia passes through the internal ring and enters the canal, but does not escape from the external ring, it forms an *incomplete inguinal hernia*. If it continues and projects through the external ring, it forms a *complete inguinal hernia*. If it continues and descends into the scrotum, it is further described as a *scrotal* or *inguinoscrotal hernia*. If the protrusion occurs from the external abdominal ring without having traversed the inguinal canal, the hernia is called a *direct inguinal hernia*. If the viscera descends through the canal, the condition is described as an *indirect inguinal hernia* or an *oblique inguinal hernia*. In women, in whom inguinal hernia is more rare than in men, the protruding viscus descends into the labium majorum, forming an *inguinolabial hernia*.

According to the relation of the protruding viscus to the deep epigastric artery, inguinal hernia is further classified into the *external inguinal hernia* if external to the artery, and *internal inguinal hernia* if internal to it.

When the vaginal process of peritoneum remains open, so that the peritoneal cavity and cavity of the tunica vaginalis testis remain one, the intestine is at liberty at any time to descend into the scrotum in relation with the testicle. This imperfect development permits the occurrence of what is described as a *congenital inguinal hernia*. If, however, the funicular portion of the vaginal process alone remains patulous and the intestine descends into the scrotum, it cannot be in immediate relation with the testicle, because the cavity of the tunica vaginalis testis is separated from the peritoneal sac in which the gut is contained. The descending intestine is, therefore, obliged to push aside the tunica vaginalis as it descends. Such a condition is known as an *infantile inguinal hernia*.

If the funicular portion of the tunica vaginalis testis remains open for a considerable height, so that the cavity of the tunica vaginalis testis is much larger or longer than normal, a hernia descending into the scrotum through the open vaginal process invaginates the funicular process and forms a double covering of serous membrane. A hernia of this peculiar formation was described by Cooper as an "*encysted hernia of the tunica vaginalis testis*," and by Hey, of Leeds, as "*infantile hernia*."

Femoral hernia is more common in women than in men. It is formed by the escape of the viscera from the femoral canal on the upper inner aspect of the thigh. It projects just below Poupart's ligament in the line of the femoral vessels.

Umbilical hernia occurs in children and in adults with relaxed abdominal walls. The viscera escape from the umbilicus.

Obturator hernia, hernia of the foramen ovale, or **infrapubic hernia**, is caused by the escape of the viscera through the *obturator foramen* of the hip-bone. The course of the intestine is outward along the obturator artery and nerve. This form of hernia is rare.

Ischiatic hernia or **sciatic hernia** consists of an escape of the intestine through the great sacrosciatic foramen. It is of infrequent occurrence.

Perineal hernia or **ischiorectal hernia** is a rare form in which the intestine escapes through a separation of the fibers of the levator ani muscle, in front of or beside the anus.

Labial hernia or **pudendal hernia** is also infrequent in occurrence, and consists of a descent of the intestine between the vagina and the ramus of the ischium into the labium majus.

Vaginal hernia, very rare, is formed by the descent of the intestine between the uterus and rectum. The projection occurs upon the posterior vaginal wall.

Lumbar hernia consists of a protrusion of the intestine through Petit's triangle, the space bounded by the crest of the ilium, the external oblique, and latissimus dorsi muscles.

Abdominal hernia is an indefinite term used to describe the escape of the intestine through the muscular walls in consequence of operation wounds, injuries, or disease of their tissues.

The internal hernias are of much interest. The most frequent form is probably that in which the intestine passes through an opening in the mesentery—*mesenteric hernia*. The mesenteric openings are probably congenital defects in most cases, though they may result from disease. More rarely the hernia occurs through openings in the omentum.

Hernia of the foramen of Winslow, by which the intestines passing through the foramen of Winslow transfer their position from the greater to the lesser peritoneal cavity, is also occasionally seen.

In *diaphragmatic* or *phrenic hernia* the viscera pass from the abdominal into the thoracic cavity as a result of congenital defect or disease of the diaphragm. It may also occur in consequence of enlargement of the natural openings and defects in the central tendons of the diaphragm. The spleen sometimes enters the thorax in these cases, likewise the stomach, and even the liver. The organs may be covered with sacs derived from the peritoneum or pleura or may lie free in the thoracic cavity.

Acquired diaphragmatic hernias are the result of perforating wounds. They usually occur on the left side, as the liver protects the right side and prevents the escape of the intestines.

Retroperitoneal hernia is formed by the entrance of the intestines into the fossa duodenojejunalis, the fossa intersigmoidea, and the fossa subcæcalis.

Properitoneal hernia consists of the entrance of the intestine into the space between the peritoneum and the anterior abdominal wall. It is also sometimes called *parainguinal hernia*.

According to their contents, hernias receive various names. An *enterocele* contains some portion of the intestine; an *epiplocele*, or *omental hernia*, a part of the omentum; a *cystocele*, or *cystic* or *vesical hernia*, a part of the bladder; a *cecal hernia*, or *cecocele*, contains a part of the cecum; a *hysterocele* contains the uterus; a *rectocele*, part of the rectum.

According to the freedom with which the viscera enter and exit, hernias are divided into:

1. **Reducible**, in which their contents can be returned to their normal relations.

2. **Irreducible**, when the contents cannot be returned to their normal relations. Surgeons make two classes of irreducible hernias: (1) The *temporarily irreducible hernia*, in which the return of the contents is interfered with by collections of gas, feces, etc.; (2) *permanently irreducible*, in which inflammatory adhesions or other permanent conditions make it impossible for the intestine to be returned.

3. **Incarcerated hernia** is a form of irreducible hernia in which collections of fecal matter or foreign matter unable to escape from the contained intestine not infrequently cause obstruction of the bowels.

4. **Inflamed Hernias.**—Hernias may become inflamed from external injury, as from ill-fitting apparatus worn to support the tissues, or from various causes associated with the intestinal contents. Inflammation is always a serious matter, as it is likely to result in the formation of adhesions between the gut and its sac which transform a reducible into an irreducible hernia. Suppuration occurs in rare cases, which are spoken of as "*suppurating hernia*."

5. **Strangulated Hernias.**—Strangulation is the most serious accident that can happen to a hernia. It depends upon the constriction and obstruction of the blood-supply and consequent devitalization of the tissue, resulting from pressure at some part of the hernial sac.

Strangulation seems to be purely mechanical, and results from the pressure exerted upon the intestine by the tissues through which it passes, or by the neck of its sac, or by fibrous bands formed in consequence of inflammation, or by combinations of these. As, however, every hernia escapes through some opening with fairly resisting walls, and as every hernia is surrounded by its sac, and as many hernias are bound by cicatricial bands, the interesting question arises, why some, but not all, hernias strangulate, and why a hernia which has already existed for years without strangulation will occasionally unexpectedly strangulate, with fatal result. The probability is that strangulation depends upon changes in the relation of the hernia to its surrounding tissues, which are then compelled to exert detrimental pressure upon it. These changes are probably simple—in many cases are probably no more than the collection of an unusual quantity of gas or fecal matter in the invaginated portion of intestine.

The strangulated intestine soon falls into a condition of passive hyperemia, becomes edematous, discolored, and swollen; these conditions all further increase the prevailing prejudicial conditions, and lead to changes in the organ, which may finally become gangrenous. Its functions are early suspended, and obstruction of the bowels is one of the earliest symptoms.

The time required for the destructive changes is variable—slow in some cases, rapid in others. Sometimes a few hours will suffice to bring about gangrene.

The appearance of the strangulated intestine will vary with the stage reached. In the stage of congestion the organ appears swollen and red, but soon becomes dark and purplish in color, with numerous hemorrhagic infiltrations beneath the serous coat. Later, the whole invaginated portion becomes deep purple or dark reddish-brown in color, the surface is usually ecchymotic, and the consistence leathery. When gangrene makes its appearance, it becomes easily lacerable, darkly discolored, and fetid. Inflammatory exudation with fibrinous deposit usually occurs, and seals the neck of the sac to the constricted portion of the organ.

The usual outcome of strangulation is death, but in rare cases the gangrenous portion of the intestine sloughs off and escapes through an external wound. Inflammatory adhesions protect the abdominal cavity from infection, and the patient recovers with a fecal fistula at the seat of the disease.

The formation of a hernia, whether through one of the natural openings or through an imperfectly closed wound, etc., is always preceded by the protrusion of a bag-shaped pouch of peritoneum which surrounds the hernia and forms its *sac*. The sac is usually narrow at its origin, especially when large, where a distinct *neck* is formed, and capacious at its distal portion. The size varies with the hernia, sometimes being insufficient to admit a loop of intestine, only allowing a portion of its wall to enter—*Littre's hernia*, sometimes large enough to contain nearly all the intestines and some of the other viscera. Except when previously inflamed or incarcerated, the hernia is freely movable within the sac, which, like the peritoneal cavity itself, contains a little fluid, so that it is perfectly lubricated. Rarely this fluid increases to form a large cystic dilatation—*dropsy* or *hydrocele* of the hernial sac. In the inguinal and femoral regions especially, but also elsewhere, there is an infundibular fossa above the entrance to the hernial sac. In this the intestines habitually lie, and their descent from it into the sac is made easy.

As acquired hernias become older, the opening through which they pass becomes larger, the tissues being gradually separated and the fat absorbed. Not infrequently, however, the surrounding tissue becomes somewhat cicatricial, so that a tendency to contract is observed and may aid in bringing about strangulation.

Hernia probably never recovers spontaneously, the conditions under which it exists tending rather toward continued increase in size than toward recovery.

The continued pressure of a truss may, however, be followed by inflammatory changes in the empty sac which lead to obliteration and make it impossible for the hernia again to escape from the original orifice.

Hernias are described by anatomists as *congenital* and *acquired*. This really refers more to the conditions favorable to their formation than to their actual existence, for it is quite correct to speak of a hernia formed in adult life through a congenitally existing passage from the abdominal cavity to the tunica vaginalis testis as a *congenital hernia*.

Hernias are also said to be of slow or rapid formation, according to the length of time during which they form.

OBSTRUCTION OF THE INTESTINES.

Etiology.—The intestine may be obstructed by the accumulation of a normal contents. This is seen, in rare instances, among those who have carelessly swallowed large numbers of cherry-stones, melon-seeds, and similar, usually harmless, bodies. In equally rare instances the intestine has been found completely obstructed by a number of gall-stones simultaneously discharged from the gall-bladder.

Intestinal parasites rarely cause obstruction, but cases are on record in which tangled masses of round-worms have formed a complete barrier to the passage of the contents.

Such conditions are serious, but are less frequent than obstructions depending upon changes in the intestine itself.

Foreign bodies in the intestine usually enter by the mouth. All imaginable objects, from grape- and cherry-stones to false teeth, roller bandages, and tacks, may be swallowed and cause obstruction.

Occasionally the foreign bodies are introduced through the rectum. In either case the damage done will depend upon the size of the body and its ability to pass through without impaction.

Volvulus.—Volvulus is a twist of the intestine by which it becomes obstructed. There are two kinds of intestinal twist : *first* and most frequent, that in which the intestine rotates upon its long axis and produces a combined twist and kink, and, *second*, that in which a link of intestine is twisted in much the same manner as the handkerchief used as a tourniquet.

The first form is usually seen in the ascending colon, in which the mesentery is absent or very short, while the other is chiefly met with at the sigmoid flexure, where the mesentery is long. Volvulus is seen almost exclusively in the large intestine, but I have seen a case of volvulus of Meckel's diverticulum that produced a fatal result. It is most frequent in persons between thirty and forty years of age.

In the first form of volvulus it is probably more the kink than the twist that causes the obstruction, and the obstruction may be incomplete. In the second the pressure of the one portion as it twists about the other completely obstructs it. The affected part of the intestine becomes congested, inflamed, and, if the condition persists, may become gangrenous. It is frequently fatal.

The cause of the volvulus is very obscure. A long mesocolon predisposes to it, and powerful peristaltic movements may influence it. It is, however, largely an intestinal accident.

Intussusception or **invagination** is the entrance of one part of the intestine into another. It is nearly always an upper portion that enters a lower. The classic description used to make the condition clear to the student's mind is that of a glove-finger which, during removal, is shortened by being drawn into itself without being inverted. The diseased portion of the intestine usually forms a cylindric tumor, which, when examined, proves to have three complete coats. The outer has been called by Rokitansky the *intussuscipiens*, or sheath; the remainder, the *intussusceptum*.

Of 295 intestinal obstructions collected by Fitz, 93 depended upon intussusception. Of the 93 cases, 52 were in males and 27 in females. Of 293 cases collected by Pilz, 158 occurred in the first year.

The condition is most frequent in early life; more than one-third of the collected cases occurring during the first year of life, and more than two-thirds during the first decade.

The invagination occurs at various portions of the bowel, but, as is shown by the cases collected by Leichtenstern, has a marked predilection for certain seats.

Ileocecal invaginations	212	(44 per cent.)
Ileum into ileum	142	(30 per cent.)
Colon into colon	86	(18 per cent.)
Ileum into colon	39	(8 per cent.)

The most frequent seat is the ileocecal valve, where some inches of the ileum may pass into the cecum. Enough of the small intestine may enter to reach far into the colon, having in rare cases drawn the cecum after it into the lower bowel until the intussusceptum reached to the rectum. The ileum may enter the ileum, or the colon, the colon.

The cause of the invagination is uncertain. Leichtenstern suggested that it depends upon vigorous peristaltic movements in one part of the bowel, immediately below which the organ is paralyzed. Its clinical causes almost certainly have to do with irregularities of peristalsis, as is suggested by the fact that it occurs at an age when peristalsis is very active, follows diseases associated with marked or irregular peristalsis, and has an undoubted analogue in the agonal invaginations of young babies.

The intussusceptum does not enter the intussuscipiens alone, but carries with it its mesentery, which is pressed upon by the sheath, so that there is marked interference with the circulation. The invaginated gut may slip out spontaneously, but, as a rule, the peristaltic movements become more and more active because of the obstruction, and the tendency always is for the invagination to increase rather than to diminish in size.

The persistent pressure upon the blood-supply of the inner segment, and the swelling which follows, as well as the presence of the invaginated portion of intestine, causes complete obstruction of the bowels.

The changes that follow invagination are very interesting as illustrating the ability of the organism to care for itself.

The intussusceptum, from passive congestion, loss of nutriment, and pressure, becomes congested, edematous, inflamed, and gangrenous as time goes on. Inflammation brings about union of the serous surfaces of the upper edge of the sheath and the contiguous part of the healthy intestine, and it is quite possible after these adhesions have formed for the invaginated link of intestine to slough off and be passed by the rectum, leaving a wound united as neatly as the best surgeon could do it. Recovery by this means is, unfortunately, very rare, as the disturbance ends in reversed peristalsis and the patient succumbs to exhaustion or dies from peritonitis or other causes. According to Widerhofer, of 46 cases in children in which a hopeful outlook resulted from separation of the intussusceptum, only 27 recovered.

In a case of recovery after intussusception that took place in a little child aged eight years, the sloughs which separated were sent to me by Dr. McCaa, who attended the patient, and consisted of quite a fragment of the cecum and the entire vermiform appendix.

Stenosis of the Intestine.—Narrowing of the lumen of the intestine, with consequent incomplete obstruction, may result from a variety of causes, none of which is very common. *Cicatrices resulting from ulcerations* are first in importance. They occur after traumatic lesions, as a result of syphilis and tuberculosis, and much more rarely from the ulcers of typhoid fever. The morphology of the ulcers may explain the different conditions following cicatrization. Thus, the elongate form of the typhoid ulcer prevents its causing stenosis. It is, however, to be remarked that typhoid ulcers produce little cicatricial tissue, the cells of the lymphatic tissue proliferating so as to replace that lost. Tuberculous ulcers are irregularly rounded and oval, and have their longer diameters transverse to the intestine, so that cicatrization may be followed by constriction. Severe attacks of dysentery may also be succeeded by stenosis from contracting cicatrices.

Cancer of the intestine, of whatever form, but especially the cylindric epithelioma, is almost certain to be followed by marked connective-tissue formation, contraction, and stenosis. Lesions of this kind are usually found in the large intestine, at the ileocecal valve, sigmoid flexure, or elsewhere.

They form annular tumors of small size, but greatly reduce the caliber of the gut.

Compression of the intestine by fibrous bands, adhesions, etc., and by morbid growths of other organs may also lead to stenosis.

Dilatation of the Intestines.—Dilatation is the natural outcome of incomplete obstruction, and is most frequent in obstructions of the large intestine. The fecal and gaseous matters collect in the proximal part of the organ and lead to dilatation, which varies in extent according to circumstances. The dilated bowel is apt to undergo some atrophy of its walls, and becomes unable to maintain the violent peristaltic movements necessary to express the contents through the small opening, so that they remain and decompose and favor further dilatation. The condition is called *coprostasis*. Chronic constipation with fecal impaction may produce dilatation of the bowel, with atrophy of the muscular tissue and inability to cope with the inspissated contents. An example of such dilatation has been reported by Formad. The case was a man accustomed to exhibit himself in museums as the "human bass-drum." The abdomen of this man was immensely distended from the presence of a colon as large as that of a horse. Formad's view of this case was that the dilatation was the primary condition and not the result, but rather the cause, of coprostasis.

Diverticula of the Intestine.—Partial dilatation in the form of incomplete diverticula or pouches are not infrequently formed. The most interesting diverticula that I have seen occurred low down in the sigmoid flexure, and consisted of a double series, one on each side of one of the longitudinal muscular bands. Each was about a centimeter in diameter, communicated with the bowel by a small opening, and contained a small, rounded mass of inspissated fecal matter.

CONGESTION OF THE INTESTINES.

Acute congestion usually results from the action of irritating substances contained in the intestine or from infection.

Passive congestion of the intestine is frequent in cirrhosis of the liver and in other conditions associated with engorgement of the portal system. The condition is usually general to the entire organ, but is not so conspicuous in the intestine as in the stomach. Local passive congestion of the intestine may result from thrombosis of the veins, or, as is more frequent, from compression of the organ from any cause. When intense, as in strangulated hernia, the part affected is dark blue in color, swollen, slightly roughened, and thickened.

Passive congestion is sometimes followed by *edema*, a condition which is not very frequent, and which causes the organ to swell and become boggy.

In congestion of the intestine from pressure the chylous vessels are also obstructed and turgescent, and the formation of little submucous chylous cysts is not uncommon. When these minute cysts are numerous and closely approximated, one often receives the impression that a lymphangiomatous change is present.

Embolism and **hemorrhagic infarction of the intestine** are sometimes seen. The affected loop of the organ is found to be in a blue-black, bloody, infiltrated condition. The usual outcome is necrosis, which may be fatal.

Hypertrophy of the Intestine.—In obstruction of the organ the muscular walls sometimes thicken, to aid in discharging the contents, but oftener more or less atrophy and dilatation take place.

Atrophy of the intestine is rather frequent, especially at the cecum, where it probably follows attacks of inflammation. It may be limited to the mucous membrane affecting the glandular tissue, causing their cells to disappear and the mucosa to become thin, or the muscular coat may also be affected.

Amyloid disease of the intestine is of not infrequent occurrence.

It affects chiefly the connective tissue of the blood vessels in the mucosa and submucosa, but is occasionally seen in the muscular coat. The amyloid tissue appears pale and is sometimes harder and firmer than normal.

Fatty degeneration and **hyaline degeneration** are occasionally observed in the muscular coat of the intestine.

Pigmentary infiltration of the muscularis is not infrequently seen in senile cadavers in the form of yellow granules in the muscle-cells. They may be so plentifully distributed as to give the intestine a yellow-brown color. The pigment does not contain iron.

INFLAMMATION OF THE INTESTINE (Enteritis).

Inflammation of the intestine may affect the small intestine (*enteritis*), the large intestine (*colitis*), or both (*enterocolitis*). As the causes of enteritis frequently find their way into the intestine from a previously inflamed or irritated stomach, the inflammations of the upper part of the organ are commonly associated with inflammations of the stomach, and are correctly called *gastro-enteritis.* Inflammation of the lower part of the small intestine is nearly always associated with associated disease of the large intestine and forms an *enterocolitis.*

Local inflammations of any particular part of the canal, for purposes of accurate localization, are called *duodenitis*, *jejunitis*, *ileitis*, *cecitis* or *typhlitis*, *appendicitis* or *scolecitis*, *colitis*, and *proctitis.*

Etiology.—Enteritis may depend upon extrinsic and intrinsic causes.

Extrinsic Causes.—The intestine may be subject to the *traumatic injury* of foreign bodies which have been swallowed and entered through the natural openings, or which have found their way into it by ulceration of its wall. In the former group must be placed unmasticated and indigestible foods, tacks, bits of glass and tin, seeds and stones of fruits, etc. ; in the latter, gall-stones and similar bodies which form in neighboring viscera and work their way by ulceration into the intestine.

Irritative chemical substances, especially those of caustic action (mineral acids, carbolic acid, corrosive sublimate, nitrate of silver, etc.), when swallowed, exert their effects upon the intestinal wall and produce lesions of varying severity and extent. Certain poisonous substances absorbed from the stomach and upper intestine are eliminated by the lower intestine and colon, where they provoke inflammations.

Infectious agents are among the most important causes of enteritis. The possibility of some reduction of vital resisting power of the epithelial tissues, or of some unusual quality of the intestinal contents, or the association of newly introduced bacteria, effecting an increase in the biologic peculiarities of the normal bacteria of the intestine, leading to irritation and inflammation, is not to be forgotten. The occurrence of insignificant lesions of the intestinal wall with infection by bacteria, usually not important, seems to be a fruitful source of danger in appendicitis. The presence of unusual bacteria with markedly infectious powers, such as the streptococcus, typhoid bacillus, Bacillus dysenteriæ, cholera spirillum, tubercle bacillus, etc., may occasion extensive and characteristic lesions.

Hematogenous infection of the intestine may also occur in cases of pyemia ; lymphogenous infection in inflammatory disease of the peritoneum and neighboring viscera.

Parasites developing in the intestine and irritating its wall by their movements, by slight traumatic lesions, or by secreted irritative metabolic substances, may occasion inflammatory reactions, the Amœba coli probably deserving the first place among these.

Intrinsic Causes.—Under this heading are included those irritants which are formed in the body by its metabolic processes, and act upon the intestine during elimination. Unfortunately, knowledge upon this subject is as yet too vague to permit much discussion. The best known elimination of this kind occurs in certain forms of nephritis with uremia, in which diarrhea, evidently of elimination, occurs. In certain extrinsic poisonings toxin elimination is also well shown.

Any inertia of the rectum or colon leading to *coprostasis*, or lack of secretion of the intestinal glands, by which the feces are retained and become abnormally dry, hard, and irritating, may be called an intrinsic cause of inflammation.

It cannot be shown that age, sex, heredity, social condition, occupation, or racial conditions have any particular influence in the etiology of enteritis, except those arising from environment. Thus, children suffer from a very severe and often fatal form of enterocolitis known as *cholera infantum*, which seems to depend upon poisons (ptomains) in the milk of which they partake. The same condition develops in adults when in "ice-cream poisoning" the same ptomain, *tyrotoxicon*, is taken. Occupations in which workmen have to handle such poisons, as lead, mercury, or arsenic, may be particularly dangerous, the well-known "lead colic" serving as an illustration.

1. **Catarrhal Enteritis.**—This form of enteritis presents very few anatomic changes. The hyperemia that characterizes most inflammatory lesions may be entirely absent, or if present, may be noticeable only upon the apex of the folds of mucous membrane as a delicate pinkish blush. In the intestines of infants dead of enterocolitis the mucous membrane frequently appears unusually pale. The contents of the bowel are fluid, showing that exudation has been active, and upon the mucous membrane an unusual quantity of mucus may be observed. The Peyer's and solitary lymphatic collections may be enlarged. Occasional erosions of the epithelium may be found. Submucous petechiæ and ecchymoses are not infrequent, and sometimes appear quite distinct because of the contrasting pallor of the rest of the intestine. Occasional epithelial exfoliations take place in the form of shreds.

When the wall of the intestine is examined microscopically, the mucosa is found infiltrated with leukocytes, the lymphatic tissue is increased in quantity, there are an abnormal number of goblet cells in the epithelium that has not exfoliated, and small cysts with mucous contents may be noticed here and there. A good many "mastzellen" are sometimes present in the submucous tissue.

2. **Follicular enteritis** is characterized by the addition of a very marked enlargement of the solitary lymph-follicles throughout the intestine. They appear swollen and project from the surface of the mucous membrane, their pale color contrasting with the rest of the mucous membrane if there is any hyperemia. Follicular enteritis is frequent in children as part of the pathology of enterocolitis, and also occurs in death from diphtheria. In rare cases in which the follicles are definitely infected suppuration may occur and lead, by evacuation, to the formation of ulcers. The enlargement of the Peyer's plaques in follicular enteritis depends upon hyperplasia of the lymphoid tissue, the entire plaque being dotted by the enlarged single follicles, a reticulum of normal and fibrillar tissue passing between them. The early stages of typhoid fever show an exaggeration of the lesions of follicular enteritis.

When the intestinal wall is subjected to microscopic examination, the lymphoid tissue is found to be universally increased in amount, and the lymph-follicles hyperplastic. About each follicle more or less round-cell infiltration is observed, and it is more than probable that infection is the cause of all the changes.

Follicular enteritis may develop from the catarrhal and lead directly into the ulcerative form.

3. **Pseudomembranous enteritis** usually occurs in the large intestine, though it sometimes extends into the ileum. The formation of the pseudomembrane begins upon the summit of the valvulæ conniventes and other folds of the mucous membrane. The pseudomembrane appears of a grayish color, and consists of a slough of necrotic epithelium with an abundance of round-cells, mucus, fibrin, bacteria, etc. The membrane is rarely tenacious, but usually soft and pulpy. As it shreds off, or in rare cases exfoliates, in large pieces or cylinders, the surface is left denuded and exposed, as well as infected, and soon ulcerates.

When examined microscopically, the mucosa is found profoundly altered by round-cell infiltration, superficial necrosis, and inflammatory exudation.

The intestinal wall is in a condition of inflammatory edema, infiltrated throughout with leukocytes, and in the lymph-spaces collections of bacteria and in the dysenteric cases amebæ are present. The capillaries and sometimes larger vessels are thrombosed. Between the pseudomembranous areas the mucous membrane is hyperemic, edematous, thickened, and infiltrated with round-cells.

If the condition depends upon the action of caustics and the patient lives, the regeneration of the lost membrane readily takes place and the ulcers cicatrize.

The pseudomembranous enteritis, by the separation of the gangrenous superficial sloughs, always becomes ulcerative, and some of the most serious ulcerative forms begin as pseudomembranous colitis.

The infection of denuded areas of the surface is sometimes attended with a rapid phlegmonous inflammation (*phlegmonous enteritis*) by which large areas of mucous membrane may be dissected loose and destroyed.

Beneath these, or such remnants of them as remain after evacuation and exfoliation have gone on, communicating sinuses can be found.

4. **Ulcerative enteritis** may result from infection and suppuration of the lymphoid follicles in catarrhal and follicular enteritis, especially in typhoid fever, from the separation of pseudomembranous sloughs in dysentery, and from pyemic, tuberculous, syphilitic, and other local affections.

The ulcers may be superficial and embrace only the mucous membrane, or they may be deep and include other coats, even to the extent of perforation. In some cases the ulcers are covered with healthy granulation tissue, and regeneration proceeds uninterruptedly after the exfoliation of the sloughs or evacuation of the abscesses. In other cases the ulceration, because of continued infection, assumes a phagedenic course and extends, undermining the mucosa, as in dysentery. Sometimes very feeble efforts at cicatrization occur, as in tuberculosis, sometimes marked cicatrization and contraction, as in syphilis and dysentery. The appearances of the ulcers occurring in the special diseases are usually characteristic, and will be fully described under typhoid fever, tuberculosis, dysentery, and syphilis of the intestine.

Chronic enteritis depends upon persistence of the cause of irritation and continued damage of the organ. It often follows the acute forms, though sometimes, as in dysentery, it may have its essential characteristics from the start. It usually occurs in the large intestine, and is most frequent in the lower colon and rectum.

The lesions consist of connective-tissue hyperplasia, and result in thickening and fibroid changes in the walls of the organ. The mucosa is thickened, the lymphatic follicles enlarged, and the surface of the mucosa is irregularly marked by alternating cicatrices and healthy tissue. When marked contraction of the cicatricial tissue has taken place, the islands of healthy tissue project from among them.

In the healthy tissue hyperplasia not infrequently takes place, and a polypoid condition similar to that seen in chronic gastritis is found. The surface of the mucous membrane is covered wtth grayish mucus, which may adhere tenaciously, and the chronic hyperemia accompanying the disease may cause the mucous membrane to become of a grayish, slate color, or in very marked cases deep blue-black. The vessels of the submucosa are enlarged. In the mucosa and submucosa there are considerable round-cell infiltration and connective-tissue induration. When large ulcerations have cicatrized, large cicatrices may be found, and the contraction of these cicatrices causes considerable deformity—stenosis. The contraction of the diffuse connective tissue of the mucosa and submucosa frequently leads to atrophy of the glandular tissue, and intensifies the polypoid appearance of the projecting normal tissue.

Physiology.—All forms of enteritis predispose to diarrhea by irritative stimulation of peristalsis and by increasing the intestinal secretions. They all have a marked effect upon nutrition, which becomes greatly disturbed because the food cannot be properly treated, and because poisonous products are absorbed. Typhoid fever is sometimes an exception, some cases being accompanied by constipation. This may be explained by the fact that in this disease the lesions are chiefly in the small intestine. Colitis and proctitis are invariably accompanied by diarrhea.

Special Forms of Intestinal Inflammation.—**Duodenitis** usually accompanies gastritis, and probably depends upon extension of the inflammation from the stomach to the intestines by continuity of tissue. Whenever the contents of the stomach have an abnormally irritating character, they are apt to irritate the duodenum as they enter. That the gastric secretions are not changed at once in the duodenum is shown by the fact that peptic ulcer occurs there as well as in the stomach.

Ileitis is the usual form of enteritis. It may present any of the appearances already described.

Typhlitis, or inflammation of the cecum, is in many cases entirely dependent for its existence upon appendicitis. Typhlitis may occur, however, as a primary affection depending upon the presence in the cecum of hard feces—*typhlitis stercoralis*.

If the inflammation occurs in the cellular tissue about the cecum, it is called *perityphlitis*. Most cases of perityphlitis depend upon appendicitis. When the inflammation is entirely extraperitoneal and involves the cellular tissue behind the cecum, it is sometimes called *paratyphlitis*. This condition also depends almost exclusively upon appendicitis, and the term is rarely used.

Appendicitis, scolecitis, or inflammation of the vermiform appendix, is a frequent and dangerous disease. It probably has its predisposing cause in the small size, rudimentary wall, and meager blood-supply of the appendix. If fecal matter enters the vermiform appendix from the cecum and is retained, it becomes inspissated, forming smooth, rounded, firm concretions. In the course of time, through slow infiltration with salts of the phosphates and carbonates and the precipitation of additional substance upon the original nucleus, true *enteroliths* of varying size are formed. The pressure of these calculi upon the wall of the appendix, and the ulceration and necrosis which may thus be brought about, afford the colon bacillus and streptococcus, which are nearly always present in the organ, an opportunity to establish themselves in the tissues, with the result that inflammation, followed by ulcerative, suppurative, phlegmonous, or gangrenous processes, may develop.

A few cases undoubtedly depend upon the entrance of foreign bodies, such as nut-shells, grape-seeds, gall-stones, cherry-pits, bits of glass, etc. This was at one time thought to be quite common, but is now recognized as a rare accident, and the majority of the bodies found in the appendix are enteroliths formed there. I have, however, found an inflammation of the appendix associated with the presence of two small fragments of broken glass. That changes in the blood vessels of the appendix may be a cause of appendicitis is quite certain, and I have seen an appendix at whose tip there was a conical perforation caused by an area of local necrosis closely resembling an anemic infarct. Parasites, tuberculous ulcerations, typhoid ulcerations, and other infectious diseases may have their lesions seated in the appendix and lead to more or less serious troubles by perforation or suppuration.

The disease may reach any grade of severity, and its ultimate course will depend entirely upon the extent of damage done. The mild forms of catarrhal appendicitis probably recover spontaneously when sufficient mucus, pus, or serum has collected within the organ to displace the irritating concretion. Mild degrees of suppuration no doubt also recover spontaneously, as the number of cases examined at autopsy in which disturbances of the appendix and surrounding tissues by previous inflammation will attest.

Severe cases with extensive suppuration are apt to perforate into the abdominal cavity and cause fatal peritonitis. When this does not happen, it is probably because the appendix becomes adherent to the peritoneum or to the viscera before it perforates, and the abscess develops behind a peritoneal covering. In this manner are developed pericecal and other abscesses, which may point and discharge at most unexpected places—into the intestine, into the bladder, in the right inguinal fossa, in the renal region, in the crural region, etc.

The inflammation having subsided, may recover perfectly, or the original conditions remaining, the patient may suffer from repeated subsequent attacks until the recurring inflammation shall obliterate or destroy the organ.

Indeed, in some cases the occurrence of one attack causes a predisposition to future attacks by obstructing the already inadequate outlet of the organ, by inflammatory bands which, crossing the appendix near its base, cause the retention of secretion and lead to the transformation of the free end of the organ into a cul-de-sac or even a cyst in which bacteria are free to grow, and from which infection can occur with unusual facility should occasion offer.

More usual is the obliteration of the organ by cicatricial bands and by the contraction of connective tissue formed within its walls during recovery. It is not uncommon to find the distal half of the appendix transformed to a fibrous cord.

In all cases of appendicitis the cecum is more or less involved in the inflammatory process.

Colitis, or inflammation of the colon, may depend upon the presence of dry, irritating feces. Probably the greater number of cases are infectious or toxic in nature.

Proctitis, or inflammation of the rectum, may depend upon the presence of hard, irritating feces, but is probably more often dependent upon the traumatism of foreign bodies introduced into the rectum, and specific infections, such as diphtheria, gonorrhea, syphilis, tuberculosis, etc.

Ziegler remarks a resemblance which exists between the rectum and the appendix vermiformis in that hard fecal masses and foreign bodies so frequently act as the exciting causes of disease.

The very numerous folds of the mucous membrane of the rectum, and their frequent dilatations, known as hemorrhoids, form convenient lodging-places for berry-seeds, grape-seeds, and other small foreign bodies which may provoke ulcerations, which not infrequently lead to sinus and fistula formation.

The most common changes in proctitis are hyperemia, ulceration, and cicatrization. The surface of the mucosa is apt to be covered with adherent mucus and desquamated epithelium.

The ulcerations are not very extensive, but are foci from which perirectal inflammations spread. Perirectal abscesses may rupture externally, leaving fistulas (*fistula in ano*), or may open into the bladder or vagina. Sometimes, instead of actual fistulous communications with the exterior, blind pouches are formed by the perirectal inflammations. These are spoken of by the surgeon as internal fistulas.

INFECTIOUS DISEASES.

Dysentery is an acute or subacute inflammation of the colon and rectum, characterized by inflammatory and ulcerative lesions and the occurrence of frequent small, mucous, and bloody stools.

It is of sporadic and endemic occurrence in temperate climates, and of epidemic occurrence in semitropic and tropic climates. Rarely, epidemics make their appearance in temperate climates, Japan having for many years been seriously troubled by it.

The disease seems to affect all ages, both sexes, and all social conditions, though it seems to be most frequent among those who pay little attention to the quality of the drinking-water.

Etiology.—The etiology of the affection is still somewhat uncertain, and the indications are that different forms of the disease depend upon different causes.

1. *Endemic Dysentery, Amebic Dysentery, or Tropic Dysentery.*—It is believed that this form of the disease depends upon the *Amœba coli* of Loesch (*q. v.*). The extensive investigations of some years ago seemed to establish the fact that this protozoön was present in nearly every case in the intestinal contents and in the lesions of the mucous membrane, as well as occasionally in the metastatic liver abscesses.

2. *The epidemic dysentery* seems to have an entirely different etiology, and can be referred to a bacillus discovered by Shiga. This organism is of almost invariable occurrence, has pronounced pathogenic effects upon animals, and is specifically agglutinated by the serum of immunized animals.

Bacteriology.—The *Bacillus dysenteriæ* of Shiga is about the same size as the typhoid bacillus, measuring about 1–3 x 0.5–0.8 μ. It is usually solitary, though sometimes united in very short chains. When freshly isolated, the organism stains quite easily, perhaps more deeply in the ends than at the center, with aqueous anilin-dye solutions. It does not stain by Gram's method. After prolonged cultivation, the staining becomes somewhat irregular.

The bacillus is motile and has flagella. No spores are formed. It is both aërobic and anaërobic.

The cultures of the bacillus resemble the typhoid bacillus in nearly all particulars, so that it is not necessary to describe them in detail.

Gelatin is not liquefied; sugars are not fermented; no indol is produced (Flexner found that indol was produced); milk is not coagulated. The metabolic products are slightly acid. The differentiation between Shiga's bacillus and the Bacillus typhosus is thus synoptized by Flexner: "The latter (Shiga bacillus) shows less marked motility when first isolated, and a tendency to lose motility rapidly in artificial cultivations; it displays a more uniform generation of indol; after a brief preliminary acid production in milk, it gives rise to a gradually increasing alkalinization; it is inactive to blood-serum from typhoid cases, but reacts with serum from dysenteric cases to which Bacillus typhosus does not respond."

Morbid Anatomy.—A. *Epidemic Dysentery.*—In mild cases the large intestine, together with the lower part of the ileum, is the seat of disease. It may, however, be less extensive and embrace the rectum and sigmoid flexure and part of the colon.

The mucous membrane is intensely congested and swollen, its blood vessels are injected, and the color of the tissue varies from bright red to livid. The surface is covered with blood-stained, tenacious mucus, and frequent small hemorrhagic areas occur beneath the mucous membrane. There is considerable swelling of the lymphatic tissue of the colon, the solitary follicles enlarging and then undergoing necrosis and separating from the surface, leaving ulcerations, which may be quite numerous. In these cases the loss of tissue is quite superficial, and when the disease begins to recover, the mucous membrane readily regenerates, new glandular tissue replaces that lost, and very little change from the normal remains.

More destructive cases partake of a diphtheric or pseudomembranous nature. No sharp line separates the two forms. In the more severe cases the surface of the mucosa is covered, not only with bloody mucus, but also with a necrotic layer. The glandular layer may also be affected, and bacteria from the surface extending into it may cause its cells to undergo degenerative changes, and the more superficial cells to die and be resolved into a granular débris. Sometimes the destruction is limited to the summits of the folds of mucous membrane, but may be quite extensive. Beneath the pseudomembrane the remaining mucosa and the submucosa are infiltrated with leukocytes and plasma cells. The separation of the necrotic layer upon the surface takes place in shreds and leaves abraded and ulcerated areas.

B. *Endemic or Amebic Dysentery.*—The lesions of endemic or amebic dysentery consist essentially of extensive ulcerations.

"In the earliest stage these local infiltrations appear as hemispherical elevations above the general level of the mucosa. The mucous membrane over these soon becomes necrotic and is cast off, exposing the infiltrated submucous tissue as a grayish-yellow gelatinous mass, which at first forms the floor of the ulcer, but is subsequently cast off as a slough."

"The individual ulcers are round, oval, or irregular, with infiltrated undermined edges. The visible aperture is often small compared to the loss of tissue beneath it, the ulcers undermining the mucosa, coalescing, and forming sinuous tracts bridged over by apparently normal mucous membrane."

"According to the stage at which the lesions are observed, the floor of the ulcer may be formed by the submucosa, the muscular, or the serous coat of the intestine. The ulceration may affect the whole or some portion only of the large intestine, particularly the cecum, the hepatic and sigmoid flexures, and the rectum. In severe cases the whole of the intestine is much thickened and riddled with ulcers, with only here and there islands of intact mucous membrane."

"The disease advances by progressive infiltration of the connective-tissue layers of the intestine, which produces necrosis of the overlying structures. Thus, in severe cases there may be in different parts of the bowel sloughing *en masse* of the mucosa or of the muscularis, and the same process is observed, but not so conspicuously, in the less severe forms." "In some cases a secondary diphtheritic inflammation complicates the original lesions."

The dysenteric ulcerations may cease and healing begin at any stage. More or less atrophy of the mucosa remains, together with scar formation where large ulcerations have existed. Contraction of the larger scars may be succeeded by partial stenosis. Polypoid excrescences are also formed, and are similar in appearance and origin to those of the stomach and small intestine. Cysts are occasionally formed by obstructed mucous glands.

Histology.—Microscopic examination of the dysenteric intestine shows a difference in the two forms. Flexner writes: "In their pathological histology also the acute dysenteries differ from the amebic form. The histological changes appear in the mucous membrane, submucosa, and muscularis, being most marked in the former situations. Those in the mucous membrane consist of coagulative necrosis with exudation of fibrin and polymorphonuclear cells. The fibrinous and cellular exudate may entirely replace the glandular layer, or here and there a gland may be preserved. The pseudomembrane is a close network inclosing multinuclear, often fragmented, cells. No blood vessels are to be distinguished, but a variable number of red blood corpuscles are mingled with the exudate and lie free upon the surface. The muscularis mucosæ is not always distinguishable—indeed, it is frequently lost in the exudate. The submucosa is always much altered. From the changes found it is evident that to them is chiefly due the thickening of the gut. The part most affected is the layer next the muscularis mucosæ. Here are found hemorrhages of variable size, while in the interstices of the tissues some fibrin appears. More marked, however, are cellular accumulations, which are present, not uniformly, but in irregular areas. The deeper layers of the submucosa show similar cellular infiltrations, although the amount is less striking.

"On the other hand, at these levels, the quantity of fibrin is greatly increased and hemorrhages are numerous. The character of the cellular exudate is quite uniform. Excluding the red blood corpuscles, the new cells consist of plasma cells. These are collected into foci, often about blood vessels, veins, and arteries, but sometimes occur in small groups or singly. There can be no doubt that these are identical with Unna's plasma cells; they show the reticulated nucleus, often placed eccentrically, and the fine blue granulations of cell protoplasm in eosin and methylene-blue staining. As the deeper levels of the mucosa are reached, hemorrhages and fibrin are abundant. The size of the foci of plasma cells gradually diminishes. At the muscular border they have about disappeared. Among the plasma cells a variable number of eosinophilic cells may be distinguished. In the submucosa, infiltrations, hemorrhage, and fibrin formation take place also beneath an intact or almost intact mucous membrane. The nature of the cellular infiltration may be identical with that already described, but, in addition, accumulations of lymphoid cells may frequently be seen. These exist in the layer of the submucosa immediately next the muscularis mucosæ; the deeper cells resemble plasma cells. The blood vessels of the submucosa may be patent and congested, the blood containing an excess of white elements; or they may show recent leukocytic and fibrinous thrombi. Hyaline degeneration of the vascular walls was not encountered. Large spaces in the submucosa may contain fibrinous clots; these are probably dilated and thrombosed lymphatic vessels. The muscular coat shows only hemorrhages, which may be of large size, although they are usually smaller than in the submucosa. The peritoneal tunic is usually unaltered."

In amebic dysentery the disease begins with infiltration of the submucosa, necrosis of the mucous membrane, exfoliation, and consequent ulceration. The lesions are less destructive in the epidemic dysentery, and in the endemic form the mucosa may be entirely destroyed and exfoliated over considerable areas of intestinal surface. A section through a remaining fragment shows the surface necrotic, the deeper structure intensely infiltrated with polymorphonuclear leukocytes and plasma cells, fibrin networks here and there, and all the varied changes that one would expect in a process complicated on every side with local bacterial infection, the presence of amebæ, etc.

The amebæ are found in the intestinal contents and also in considerable numbers in and between the coats of the gut.

Complications.—The chief complication of dysentery is *abscess of the liver.* The abscesses may be either minute and multiple, from the entrance of bacteria with the portal blood, or may be single and large. In the multiple metastatic abscesses bacteria which have entered from the denuded intestine are always present. In the large abscesses they are absent. The absence of bacteria and the presence of amebæ in the large or "tropic abscesses" have been used in support of the view that the amebæ are capable of exciting the inflammation of the colon, because it can produce the abscess of the liver. It is not impossible, however, that the hepatic abscess depends upon bacteria not yet discovered, or that those which caused it have died out before the lesion was investigated.

Thrombosis of the veins of the colon and mesentery and thrombosis of the portal vein may complicate dysentery, being caused by bacterial emboli.

Perforation of the colon is not infrequent in dysentery with extensive and deep ulcerations.

Stenosis of the rectum and colon may succeed dysentery, from the contraction of the connective tissue formed during the cicatrization of extensive ulcerations.

Cholera Asiatica.—Cholera is an acute epidemic, infectious, specific disease, characterized by fever, vomiting, copious diarrhea, cramps, and collapse, followed by death or recovery.

It is endemic and epidemic in India, which seems to be its natural habitat, and spreads in epidemics to neighboring and remote countries at irregular times.

According to the consensus of opinion, the disease depends upon a micro-organism—the *cholera spirillum*—discovered by Koch.

Bacteriology.—The *Spirillum choleræ asiaticæ* is an organism of slightly variable morphology, prone to show marked involution and degeneration forms. As usually seen in intestinal discharges and in fresh cultures, it is a short, slightly curved rod with round ends. The peculiar curve led to its being compared to a comma, and called by Koch the "comma bacillus." In old cultures, and especially in potato cultures, it grows into long spirals which are distinctly flexible. The comma-shaped organisms measure 1.5–2 x 0.5 μ. It is actively motile and has a terminal flagellum. It forms no spores.

The organisms stain well by the ordinary aqueous solution of the anilin dyes, but not by Gram's method. The organisms are both anaërobic and aërobic.

Cultivation.—The cholera organisms grow well upon all the artificial media, both at room-temperature and at the temperature of the human body. The vitality of the organism is not great, and it is killed at temperatures above 52° C. It also dies if desiccated, and quickly dies in artificial culture if not frequently transplanted, though sometimes it may live for months. In the fecal discharges it sometimes dies in two or three days, or sometimes it may live several weeks. It is quickly destroyed by antiseptics and germicides.

The organism can be secured by diluting the rice-water discharges and making plate cultures of the dilution.

The colonies upon gelatin appear as pale, slightly yellowish, coarsely granular points with slightly irregular contours. As they become larger their appearance somewhat suggests powdered glass. Liquefaction of the gelatin soon begins, and surrounds the colony with a halo of transparent fluid. As the liquefaction is slow, the fluid evaporates almost as rapidly as it is formed, and the colony gradually sinks into a saucer-shaped depression. The colonies may also assume a rosy hue.

Gelatin puncture cultures present a fairly characteristic appearance. The growth takes place along the entire line of puncture. Liquefaction also occurs along the entire needle-path, forming a slender canal. At the surface the growth is a little more rapid, and the liquefied area a little wider. The evaporation of the fluid leaves an air-space above. As time goes on yellowish, granular matter collects at the apex of the liquefaction. The gelatin becomes slowly more and more liquefied, until, after several weeks, the gelatin is all fluid.

Upon the surface of obliquely solidified agar-agar the growth develops with the production of a grayish, moist, slimy, shining band, not distinctly circumscribed, and devoid of characteristic appearances.

Upon *blood-serum* the growth is not characteristic.

Upon *potato* the organisms grow well, even when the reaction of the potato is acid, and produce a transparent, yellowish-brown or brownish-yellow layer.

In *bouillon* and *peptone solution* diffuse cloudiness occurs, with a pellicle on the surface. The pellicle is distinct and often wrinkled. It is made up of cholera organisms, some of long spiral form.

In *milk* the organism grows luxuriantly but produces no visible change.

Chemistry.—The organism, when freshly isolated, and even when cultivated for a long time, produces indol and nitrites. It is said also to produce a toxalbumin fatal for guinea-pigs and probably responsible for the disease in man.

Pathogenesis.—Man alone is spontaneously infected with cholera; in epidemics the lower animals all escape. The virulent cholera organism, when introduced into the subcutaneous tissue of guinea-pigs, usually causes death from septicemia. If the inoculation is made into the peritoneal cavity, a peritonitis—*choleraic peritonitis*—characterized by a serofibrinous exudation containing some pus-cells is produced.

Feeding animals with cholera organisms, as well as injecting them subcutaneously, intra-abdominally, intravenously, etc., with its cultures, all fail to produce anything resembling cholera as seen in man. Koch found, however, that if the experiment animals (guinea-pigs) were given a large dose of opium in order that their peristalsis might be checked, the gastric contents then alkalinized, and cholera cultures introduced into it, the animal, upon recovering from the narcosis, later dies paralyzed and collapsed, with the intestine filled with serous fluid and congested, the symptoms partially resembling clinical cholera.

Morbid Anatomy.—The appearance of the intestine is of interest because of its variability. Only typical cases are characteristic. In suspected cases the study of the morbid appearances alone may easily lead to error in the diagnosis of cholera.

The appearances differ with the time at which death takes place. In *early cases* the external surface of the small intestine appears of a rose-red color, sometimes deepening to purple or violet There is an inconsiderable layer of sticky fibrin upon the serosa. The same condition seems to affect other of the serous membranes, and occurs in cholera nostras as well as in cholera Asiatica. The contents of the intestine are thin and watery, cloudy, grayish, odorless, alkaline, and very abundant. When collected in a vessel and allowed to stand, a sedimentation of the little whitish flakes characteristic of the "*rice-water discharges*" occurs. Rarely is there any admixture of bile. The mucous membrane is nearly always pale and anemic, though it may be congested, and is sometimes dark-brown or red-brown in color or hemorrhagic, this being true of the lower part of the ileum especially. Shreds and flakes of mucus adhere to its surface. Koch regarded hyperemia in the neighborhood of Peyer's plaques and solitary follicles as characteristic of cholera Asiatica. When the mucosa is hyperemic and swollen, it often has a velvety appearance from enlargement of the villi.

In the early stages the plaques and solitary glands are enlarged and appear pale and conspicuous upon the hyperemic mucosa. As the disease advances the glandular swelling rapidly diminishes, the glands seem to sink deeply into the mucosa, and the plaques assume a reticulated appearance. The large intestine usually shows no signs of disease, but may be slightly hyperemic and swollen.

Histologically, the morbid changes are superficial and consist essentially in desquamation and exfoliation of the epithelium. There is also coagulation necrosis of the villi, especially at their tips, and they are sometimes destroyed. There is an absence of leukocytic infiltration of the deeper tissues, and usually very little in the mucosa. It is said that many "mastzellen" are present in the submucosa.

In *later cases*—*i. e.*, those which have passed the algid stage—the appearances are quite different. The rose color and sticky coating of the intestine disappear, and the intestinal wall is much less swollen. At this stage the intestine is found nearly empty.

Instead of the copious fluid contents, bad-smelling gas is present. The Peyer's plaques often show a slate-colored pigmentation. Secondary enteritis is very frequent in the later days of cholera, the diphtheritic—*i. e.*, pseudomembranous—form being that usually seen. Studies made during the

Hamburg epidemic indicate that the pseudomembrane is a product of coagulation necrosis of the superficial mucous membrane, especially the villous layer, which becomes transformed into homogeneous granules. The intestinal walls are more or less infiltrated with leukocytes and show many colonies of bacteria.

Sometimes the intestinal wall is infiltrated with blood, sometimes circumscribed areas of mucous membrane are covered with grayish-green pseudomembrane consisting of coagulation-necrotic tissue without fibrin. Such areas are most frequent in the large bowel.

It is to be observed that, unlike dysentery, sublimate poisoning, etc., the changes characteristic of cholera are situated chiefly in the lower part of the ileum, not in the large intestine. The large intestine often contains scybala. In unusual cases one may observe hemorrhagic gastritis or ulcerative colitis as a complication. The pathologic appearances vary in different epidemics.

Cholera nostras is an acute choleraic affection characterized by the sudden development of vomiting and diarrhea, with abdominal pain and tenesmus, and not infrequently terminating fatally. It is always sporadic, never epidemic. The "rice-water discharges" are absent. The cause of the disease is unknown.

The lesions of *cholera nostras* are nearly identical with those of cholera Asiatica. The two diseases are chiefly differentiated by the sporadic nature of the one and epidemic nature of the other, and by a bacteriologic examination.

Typhoid Fever.—Typhoid fever is an acute infectious disease caused by the Bacillus typhosus of Koch and Gaffky, and usually characterized by fever, profound nervous symptoms, diarrhea, and wasting. The most characteristic lesion is ulceration of the intestine.

Though in rare instances typhoid fever is a general infection unaccompanied by local lesions, it is chiefly an intestinal infection, characterized by a peculiar enlargement and necrosis of the lymphatic tissue.

Bacteriology.—Typhoid fever seems to be caused by the *Bacillus typhosus* of Koch and Gaffky. The bacillus is found at some time in every case of typhoid, and has almost never been found under other conditions. Its distribution in nature seems to be very limited, as outside of the diseased body it has been found but rarely and only in polluted water and foods.

Morphology, etc.—The bacillus is a distinct rod with round ends. It measures, on the average, 1–3 x 0.5–0.8 μ. Sometimes the individual organisms are very short and ovoid, sometimes long and filamentous.

The bacillus is actively motile, and has many flagella which project from all parts of its surface. These can readily be defined by Loeffler's and Pitfield's methods. No spores are produced.

The organism stains with the aqueous solutions of the anilin dyes, but not by Gram's method.

Cultivation.—The typhoid bacillus grows readily upon all the laboratory media, both at room-temperature and at the temperature of the body. It grows with and without the admission of free oxygen.

The colonies that appear upon gelatin plates are at first small, rounded, and granular. As they increase in size and come to the surface they spread out in thin, translucent, slightly bluish, iridescent films which are irregular in outline and have been compared to grape-vine leaves. The colonies never become very large, and the gelatin is never liquefied.

In gelatin punctures the bacilli grow all along the line of inoculation and upon the surface, forming a delicate, nail-like growth. There is no liquefaction of the gelatin.

Upon obliquely solidified agar-agar the bacillus forms a grayish, translucent, moist, shining, slightly spreading film. This growth has no peculiarities. On coagulated blood-serum the growth is grayish or colorless and has no characteristics.

Upon potato the typical appearance is described as the "invisible growth." The bacilli grow quite abundantly and spread out over the surface of the potato, but having no color, and, being translucent, the growth can scarcely be recognized by the naked eye, though easily picked up as a slightly viscid mass by the platinum wire.

In bouillon and peptone solutions a diffuse clouding is the only change. Sometimes a very delicate translucent serum is formed.

Milk is not altered by typhoid bacillus.

Chemistry.—The organism grows both aërobically and anaërobically.

It varies somewhat in reaction, usually producing a slight intensification of the alkalinity of the culture-media, sometimes slightly acidulating it. Often there is no change.

It does not ferment any of the sugars, and in solutions containing them evolves no gas.

It does not produce indol: it does not coagulate milk.

A toxalbumin and other toxic substances—typhotoxin, etc.—have been separated from its cultures.

Pathogenesis.—For the lower animals the typhoid bacillus is scarcely pathogenic. Only when freshly isolated and of exceptional virulence will it cause septicemia in guinea-pigs. The injection of both living and killed cultures into horses and smaller animals, however, brings about a firm, hard swelling which often undergoes necrosis and sometimes suppurates. The effects of the local lesions are sometimes fatal.

By narcotizing a guinea-pig, alkalinizing its gastric contents, and injecting some of a typhoid culture into the stomach, an infection results which bears a partial resemblance to typhoid fever in man.

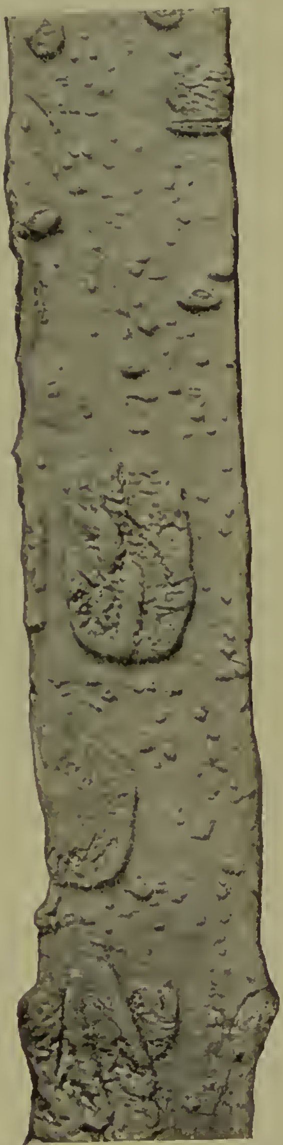

Fig. 254.—Ileum; typhoid fever (early stage); Peyer's patches and solitary follicles greatly swollen; superficial ulceration (Nicholls).

In man the typhoid bacillus not only provokes the disease known as typhoid fever, but during and after convalescence frequently occasions suppurative lesions, such as periostitis, ostitis, otitis media, osteomyelitis, meningitis, etc., and must be placed among the pyogenic bacteria.

Serum Reaction.—The best indication of the pathogenesis of the typhoid bacillus and its importance in the etiology of typhoid fever yet afforded is found in the phenomenon of agglutination observed by Widal. When brought into a 1 : 50 dilution of the blood or serum of a typhoid patient or convalescent, cultures of the bacillus quickly show a peculiar clumping, associated with loss of motion. Only the serums of typhoid patients, convalescents, and of immune animals have this effect, and it is with the typhoid bacillus only that the effect is brought about.

Intermediate between the typhoid bacillus and the Bacillus coli, a common denizen of the intestine, are a number of organisms presenting but slight cultural and biologic differences which have been called *paracolon* and *paratyphoid* bacilli. Of these, the paratyphoid bacilli seem capable of occasioning infection having clinical manifestations resembling true typhoid fever. The striking clinical difference is found in the inability of the blood of patients suffering from this infection to agglutinate the true typhoid bacillus. When isolated, the paratyphoid bacillus is found to vary from its related species in occasionally fermenting dextrose and in occasionally producing indol. The chief differential feature is, however, the inability of immune serums to react upon both species. Each serum is specific for its own organism, or acts upon it in a far greater dilution than upon the other.

Morbid Anatomy.—The lower part of the ileum and the upper part of the colon are most frequently invaded by the disease, its intensity being greatest in the neighborhood of the ileocecal valve. Sometimes almost the entire length of the intestine is involved, and the extent and severity of the lesions are remarkable. In some fatal cases the morbid changes in the intestine have been very inconsiderable, a few fatal cases being on record in which but a single typical ulceration has been found.

There is always more or less catarrhal enteritis secondary to the ulceration.

The course of the affection is somewhat protracted for an acute disease, and is briefly as follows:

The disease begins with hyperemia and swelling of the mucosa of the lower part of the ileum and a marked enlargement of Peyer's patches and the solitary glands which steadily increases, until the Peyer's patches become prominent, marked by nodes and ridges, and, finally, form large, smooth, cushiony elevations with little depressions or pits here and there upon the surface. The original hyperemia disappears from the plaques, and when largest, they become whitish in color.

The contents of the bowel are greenish-yellow, soft, and a little slimy. They contain flocculent masses and are described as being like "*pea soup.*"

During the *second week* of the disease the hyperplastic lymphatic tissue of both the plaques and solitary follicles undergoes an anemic necrosis, and exfoliation in shreds and fragments gradually takes place. The surface of the plaques at this time is covered with a thick, greenish-black slough. The necrosis and the exfoliation may apparently involve all the lymphatic elements of the follicles and plaques which seem to be cleaned out, leaving smooth bottom ulcers, but the subsequent course of events indicates that this is an error, and it is unusual to find perfectly oval ulcers. They are usually irregular and smaller than the plaques.

During the stage of necrosis a peculiar dotted appearance of the plaques often results from the more rapid disintegration of the follicular tissue than of the intermediate tissue, so that the surface becomes marked by numerous small pits in which darkened and discolored necrotic tissue contrasts with the paler surrounding tissue. To this condition the French apply the name "*plaque a surface reticulee.*" By the clinician it is often spoken of as the "*shaven-beard appearance.*" The same appearance may be due in some cases to minute hemorrhages occurring as the necrotic mass separates.

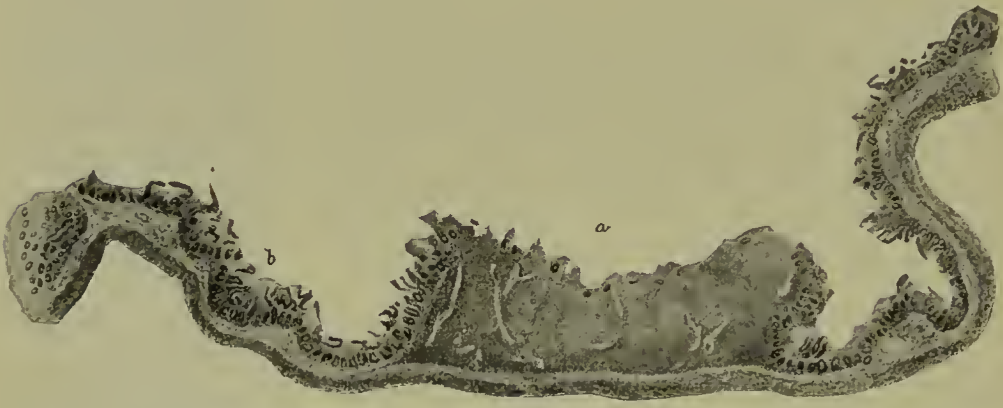

FIG. 255.—Typhoid ulceration of the small intestine: *a*, Solitary gland, greatly swollen and denuded of its covering mucosa; *b*, more normal but inflamed intestinal wall.

The necrosis reaches to a variable depth into the intestinal wall, usually involving the lymphatic tissue of the plaque only, but sometimes descending through the submucosa to the muscularis or even penetrating the muscularis and exposing the serosa. It is probable that in the greater number of cases in which perforation of the intestine occurs it is rather because the serous coat becomes involved in the necrosis than because of the pressure of feces or gas upon the thinned intestinal wall.

The necrosis of the plaques is always much more important and deeper than that of the solitary follicles.

In the separation of the necrotic mass the edges of the patch seem to loosen and shred away first. In rare cases the whole mass exfoliates and is detached at once, sometimes causing much hemorrhage from exposed blood vessels.

Sometimes a large plaque will show several irregular ulcers separated by intermediate septa.

The ulcers usually have soft, swollen, congested, sometimes excavated or undermined borders. Their surfaces soon become discolored by the intestinal contents and appear greenish or brownish in color.

The ulcers are more numerous near the ileocecal valve than elsewhere, because of the large amount of lymphoid tissue at that situation. Indeed, near this point the small intestine may have its surface transformed to one immense ulceration encircling the organ and extending upward for several inches. In such an ulcerated area small islands of healthy mucous membrane may be observed here and there. Ulcerations may also be found in Meckel's diverticulum, when it exists, and in the vermiform appendix. In the large intestine the cecum suffers more than the colon, the disease affecting the solitary glands.

About the end of the *third week* the destructive processes end. In some cases the hyperplastic lymphatic follicles and plaques are relieved of their cellular distention by degeneration and gradual absorption.

When, however, the process has gone on to ulceration, the healing is deferred because of the slow progress of cicatrization.

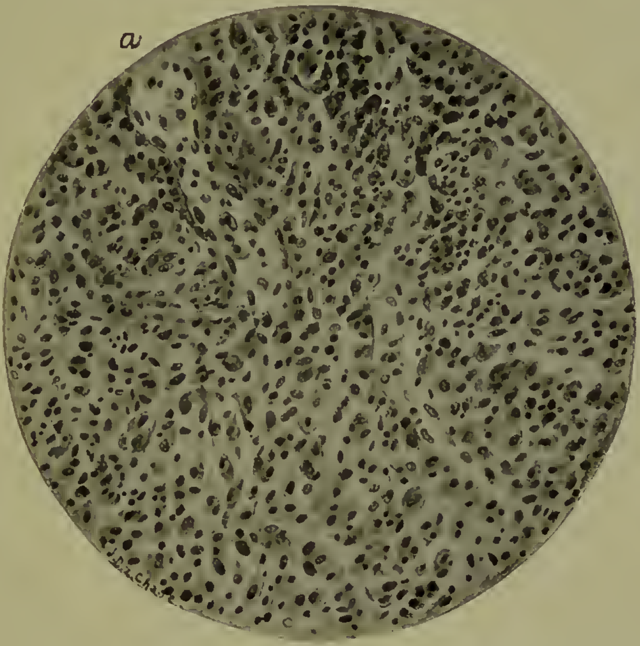

FIG. 256.—Typhoid ulcer of the intestine. The section passes through an enlarged Peyer's patch, the surface of which was necrotic. The illustration shows the ulcer to be made up of epithelioid cells, endothelial cells, plasma cells, and lymphocytes, actively growing: *a*, Blood vessel with proliferated endothelium.

In ordinary cases the destructive process is entirely over with the end of the third week, and healing usually begins in the fourth week. At this time nearly all the ulcers will be free of their necrotic shreds and found to conform more or less perfectly to the size and situation of the lymphoid accumulations—solitary and agminated glands. It is one of their most characteristic features that they do not extend beyond these confines. The duration of the cicatrization is several weeks, and in cases dying late and in relapses, it is not infrequent to see partially but not perfectly cicatrized ulcers remaining after six, seven, or more weeks. The first sign of beginning cicatrization is shown by a reduction in the size of the infiltrated border of the ulcer. Soon the mucous membrane begins to descend upon and attach itself to the denuded surface. A delicate granulation tissue forms upon the surface of the ulcer, and, by further development of the granulation tissue upon the ulcerated surface and inward extension of the mucous membrane at the periphery, the ulcer is healed, and a smooth, usually diffusely pigmented, brownish or slate-colored scar remains. Almost concomitantly with the repair of the surface a proliferation of whatever lymphoid tissue remains takes place, and before very long the plaque or follicle is again restored. While still a matter of doubt, it seems quite probable that new villi are formed by the new mucosa covering the ulcer.

The progress of events is not always so uniform and regular as described, for in some cases the process of healing begins in anticipation of the complete exfoliation of the slough, etc.

While the lymphatic tissues of the intestine are undergoing the destructive necrosis characteristic of typhoid, the neighboring lymphatic tissues are by no means exempt. The mesenteric glands always become enlarged, soften, and may rupture. When the usual course of events takes place, the necrotic part of the gland is gradually transformed into a cheesy mass which sometimes remains and may later calcify. The spleen is always enlarged.

Histology.—The increase in the cellular substance of the Peyer's patches and solitary glands was formerly regarded as depending upon a hyperplasia of the lymphoid tissue, but recent investigations by Ribbert, and particularly by Mallory, have shown this to be a mistake. According to the researches of Mallory, the typhoid bacillus produces a mildly irritative toxin, which stimulates proliferation of the endothelial cells of the lymphatic spaces, blood capillaries, and reticulum of the lymphoid tissue. These cells increase in large numbers, sometimes uniformly throughout a lymph-node, sometimes at its central or peripheral part only. The cells are large, have palely staining nuclei, acidophilic protoplasm in abundance, show frequent karyokinetic figures, and are eminently phagocytic, taking up and digesting both the lymphocytes and the erythrocytes that may be in their immediate neighborhood.

Mallory finds these cells to be the cause of all the subsequent changes, as they block up the lymph-channels, obstruct and cause thrombosis of the capillary blood vessels, and occasion the necrotic changes in the Peyer's patches, the spleen, and the liver, by thrombotic local ischemia. The cells may enter the circulation, pass through the hepatic capillary plexus, and become located in the lung, or, passing through the pulmonary capillaries, may be found in distant organs with their loads of lymphoid cells and other fragments taken up in the intestine.

Sections through the non-ulcerated Peyer's patches show the proliferative changes very well, while sections through the ulcers show the progress of the proliferation, vascular obstruction, and necrosis.

The affected lymphoid tissue is a conglomeration of epithelioid, lymphoid, plasma cells, and leukocytes in which the tracing of the inception and progress of events is difficult.

The **accidents** of typhoid fever are sometimes fatal.

1. *Hemorrhage.*—Small hemorrhages usually depend upon oozing of blood from the congested borders of the ulcerations, and merit little attention. Blood in small quantities imparts a chocolate color to the stool. Large hemorrhages usually depend upon the denudation of larger vessels by the premature detachment of large masses of exfoliating tissue. It is rarely that bright fresh blood appears in the stool, the usual appearance resulting from large hemorrhages being characterized as "*tarry stools.*"

2. *Perforation.*—The hyperplasia of the lymphoid elements may be so marked, and the leukocytic infiltration so considerable, that the necrosis embraces an unusual depth of tissue, and may even destroy the serosa.

Where the wall of the intestine has been much thinned so as to consist of a few muscular fibers and the peritoneum, passing fragments of undigested food and other solid bodies within the intestine have been known to escape from the organ into the peritoneal cavity, presumably by lacerating the delicate tissues. Round-worms have also been known to bore their way through. As is usual with intestinal perforations, if adhesions can be found with neighboring parts, the patient may escape peritonitis, but if the intestinal contents escape directly into the peritoneal cavity, death from purulent peritonitis is certain.

Metastasis in Typhoid Fever.—Typhoid fever, while essentially a local disease of the intestine, is nearly always accompanied by the escape of bacteria into the blood. Chief among these is the typhoid bacillus itself, and the regularity of its occurrence in the blood can be estimated by the constancy with which the "rose-spots" upon the skin make their appearance. Richardson has shown that these spots contain the typhoid bacilli, and it is natural to infer that they are caused by them. The bacilli also commonly appear in the urine in the third week of the disease, evidently having been carried to the kidney by the blood-stream. Ohlmacher and others have reported *meningitis* caused by typhoid fever. In the prolonged convalescence from the disease numerous remote, chiefly suppurative lesions present themselves. Among these are ostitis, periostitis, otitis, parotitis, and orchitis. The lesions are frequently occasioned by the typhoid bacillus itself, but may be caused by the colon bacillus and other micro-organisms which, having succeeded in gaining entrance into the tissues through the typhoid lesions, and finding the tissues in a condition of depressed vitality, succeeded in effecting a footing.

Relapse in typhoid fever is a repetition of the original disease. It has no etiologic or pathologic peculiarity. In the intestine the newer lesions occur simultaneously with the partly healed lesions. The ulcerations in relapse involve lymphoid tissue which escaped the primary infection, and sometimes also involve the partly healed lesions.

Associated Infections.—The most frequent complicating infection of typhoid fever is *pneumonia*, to which the patient seems to be predisposed by the general vital depression. The pneumonia is usually caused by the pneumococcus. *Noma* also occasionally results from oral infection during the febrile stages with sordes and rhagades and the dry brown tongue.

Paratyphoid fever presents lesions which the few autopsies that have been made show to differ slightly from those of typhoid. Thus, though the septic invasion of the body is much the same and the enlargement of the spleen similar, the intestinal lesions are non-specific in character. In some cases there have been no intestinal ulcerations, in others irregular and atypical ulcers situated in the lower eight or ten centimeters of the ileum, not confined to the lymphoid tissue, not accompanied by enlargement of Peyer's patches, or swelling of the mesenteric glands.

Tuberculosis of the Intestine.—Tuberculosis of the intestine occurs as a primary affection in infancy. It is very frequent as a secondary affection in adults suffering from pulmonary and laryngeal tuberculosis with tubercle bacilli in discharges which are easily swallowed, so that in almost every case of chronic pulmonary tuberculosis some infection of the intestine can be expected.

Etiology.—The disease seems to depend almost entirely upon direct infection by swallowed tubercle bacilli. In infants the bacilli are probably most frequently contained in tuberculous milk; in adults, in swallowed sputum.

The disease seems to assert itself first in Peyer's patches and in the solitary glands, but may occur anywhere upon the surface of the intestinal mucosa.

The primitive lesion is the miliary tubercle, which soon surrounds itself with an area of cellular infiltration and causes the formation of a small, rather circumscribed swelling. Coagulation necrosis occurs, and the cheesy center exfoliates, leaving a small ulcer with markedly infiltrated borders and a grayish-yellow, crumbly material showing at its base. As the lesion becomes older and larger by the addition of new tubercles, numerous outlying tubercles are observed along the lines of the lymphatic vessels, especially upon the serous surface. These extend laterally and pave the way for the increase in size of the original lesion, which, unlike the typhoid ulcer, does not conform to the shape of the Peyer's patch, but tends to spread irregularly in all directions. One of the peculiarities of the ulcer is its tendency to extend across the intestine instead of along its length, this tendency depending upon the fact that the lymphatics encircle the intestine. The outlying lymphatic tubercles are often connected by whitish cylinders, probably representing lymph-vessels which are plugged by purulent accumulations or by cheesy matter. The ulcers are usually situated at the lower part of the ileum, not far from the ileocecal valve. They may be single or multiple. I have seen a case of death from purulent peritonitis following perforation of a single tuberculous ulcer not more than 3 cm. in diameter. On the other hand, the ulcerations may be very numerous.

The lesion is rarely limited to the mucosa, but usually also involves the submucosa, not infrequently the muscularis, and sometimes the serous coat. Perforation is the chief danger to be feared, though few of the ulcers perforate, probably being prevented by the formation of inflammatory adhesions. Not infrequently the perforation occurring after the formation of adhesions between the intestine and the viscera or abdominal wall gives rise to cold abscess instead of peritonitis.

Tuberculous peritonitis occasionally results from intestinal tuberculosis.

The general tendency of the ulcer is toward continued growth and extension. Some cases show cicatrization, and a few, marked induration and thickening of the subjacent and surrounding tissues. Intestinal tuberculosis occasionally recovers, the lost tissue being replaced by a dense fibrous scar. Stenosis of the intestine may be caused by the cicatrization of tuberculous ulcers, the transverse direction of the tuberculous ulcer decidedly predisposing to subsequent constriction of the intestine in cases in which cicatrization occurs.

Syphilis of the Intestine.—Intestinal syphilis is uncommon. It may be acquired or hereditary. In the former case it usually finds its seat in the lower part of the rectum. The primary lesions may depend upon direct inoculation and consist of a chancre. The secondary lesions consist of mucous patches and papules; the tertiary lesions of mucus or submucous gummata, with undermining and destruction of the mucosa, so that from the anus to an altitude of several inches the rectum may be denuded, except for occasional partially attached shreds and islands of mucous membrane. The deeper structure of the rectum may also be affected in a most destructive manner, and occasional perforations may result in perirectal abscess formation. The lesions heal with the formation of dense cicatrices, which cause stenosis.

The higher part of the intestine is rarely affected, yet small gummata may occur in any part, and, by softening, produce ulcerations which present no definite characteristics by which they may be recognized, except their tendency to heal by the formation of dense cicatrices.

Hereditary syphilis of the intestine occurs in children and usually affects the small intestine. The lesions are somewhat variable. Gummata are sometimes observed, but more frequently cellular infiltrations of the mucous tissue and submucous tissue occur, and, by degeneration, cause the formation of ulcers. The ulcerations not infrequently occur in Peyer's glands or in the solitary follicles.

Lepra, actinomycosis, and **other specific granulomata** of the intestine are of rare occurrence and scarcely merit mention. They are usually secondary, and are almost unmistakable because of the associated lesions. Primary actinomycosis has been observed in the cecum.

Anthrax in cattle is commonly of intestinal origin, the bacilli being taken into the alimentary canal with the food. The infection takes place high up in the jejunum or in the duodenum, and is characterized by blackish-red or brownish-red hemorrhagic foci with necrotic yellowish or greenish-yellow centers. The tissues of the mucosa and submucosa are in a condition of bloody edema and are hyperemic.

Enteromycosis bacteritica is a general term applied to certain infections of the intestine depending upon various bacteria which are not in a proper sense specific. Cases of *meat-poisoning* or "*botulismus*" from infected meat come in this category. The lesions vary, sometimes being simple catarrhal, sometimes croupous or diphtheritic, and sometimes ulcerative in character. Ziegler says that some of the lesions are like those of anthrax; others are like typhoid.

TUMORS OF THE INTESTINE.

The **connective-tissue tumors** of the intestine are of infrequent occurrence and of little importance. Occasionally they may become large enough to cause obstruction. Pedunculated tumors may have a kind of ball-valve action. Rarely by rupture of the pedicle the tumor may be passed from the bowel. Usually, however, the pedunculated tumors are external and dangle in the peritoneal cavity. The greater number of the connective-tissue tumors spring from the submucosa. *Myoma*, *lipoma*, and *fibroma* form more or less rounded nodular tumors. They may be single or multiple. When single, they occasionally reach the size of an apple and cause obstruction and even invagination.

Angiomata are sometimes observed upon the serous surface of the intestine. Dilatation of the lacteal vessels with the formation of cysts sometimes appears as a tumor-like mass which is known as *chylangioma*.

A peculiar tumor known as **enterocystoma** is occasionally seen in connection with the intestine, and seems to result from the exclusion of fetal fragments in the process of development.

Multiple cysts of the intestinal mucous membrane seem to depend upon obstruction of the lymphatic vessels.

Sarcoma of the intestine is quite rare. The tumor seems to develop from the submucosa, and spreads rapidly, elevating the mucosa, but not causing stenosis. Round-cell sarcoma is the usual primary form. Sarcoma is sometimes with difficulty differentiated from the lymphatic enlargements of the intestine seen in leukemia and Hodgkin's disease.

Endothelioma of the peritoneum starting in the omentum not infrequently invades the intestinal serosa.

Secondary sarcoma sometimes occurs in the mucosa and submucosa in the form of single or multiple nodules. In cases of peritoneal sarcomatosis the serosa may be studded over with small secondary nodules.

Primary epithelial tumors of the intestine are more important and not infrequently cause death by obstipation.

Polypi of adenomatous structure, and easily mistaken for papillomata, are of frequent occurrence as a result of inflammatory disease. They occur in the duodenum, in the neighborhood of the ileocecal valve, and in the rectum, near where the cylindric cells end and the squamous epithelium begins. They are usually small, soft, pinkish, multiple, and pedunculated. When examined microscopically, they are found to consist of a delicate stroma filled with mucous glands. These little bodies probably have an inflammatory origin and result from the outgrowth of projecting shreds and islands of mucosa in the cicatrization of ulcers, etc. It is uncertain that they are related to the true papilloma, the adenoma, or the cancer.

Adenoma.—This tumor occurs infrequently either as the *diffuse adenoma* or the *polypoid adenoma*. The form is usually seen in the lower part of the rectum, where it not infrequently forms a circumferential growth made up of proliferated Lieberkühn's glands.

The polypoid adenoma or soft papilloma is a pedunculated or sessile, circumscribed growth from the mucosa, covered all over with a cauliflower-like mass of villous projections, while the solid part consists of proliferations of the mucous glands. This form is also most frequent in the rectum. The tumor is delicately nourished and apt to be injured by passing feces, so that portions of it are occasionally separated and discharged with the feces. When abraded, the tumor is apt to bleed slightly.

Carcinoma.—The intestinal carcinoma is a cylindric epithelioma. The tumor is most frequent at the cecum, the hepatic, splenic, or sigmoid flexure. It usually forms an annular mass, which is, as a rule, dense, firm, and contracted, so as greatly to diminish the lumen of the organ.

It may be difficult to recognize the growth as a tumor, as it closely resembles a simple fibrous ring. When the intestine is opened and examined, the tumor appears as an ulceration which is cicatricial, contracted, and distinctly scirrhous in nature. When the tissue is studied microscopically, very few epithelial elements may be found, acini here and there, lined irregularly by columnar epithelium, alone indicating the nature of the affection. Metastases are infrequent in tumors of this class, life being brought to an end through the obstruction of the intestine.

Soft Intestinal Carcinoma.—In other cases the tumor may be quite soft, and form projecting fungous masses, circumscribed, sessile, and nodular. The wall of the intestine becomes infiltrated and stiffened, but there is no cicatricial contraction. Tumors of this variety not infrequently soften and ulcerate, leaving extensive denuded surfaces which cicatrize more or less irregularly. When metastasis occurs, the lymphatic glands, peritoneum, and liver are usually affected.

The soft carcinoma is apt to occur in the duodenum at about the point of entrance of the ductus communis choledochus. They are also rather frequent in the rectum.

The intestinal carcinoma is prone to undergo mucoid and colloid degeneration—carcinoma intestinalis medullare mucosum or gelatinosum.

Microscopically, all the intestinal cancers are adenocarcinomata of the form known as cylindric epithelioma.

The medullary cancer forms a large, soft, whitish, spongy tumor, forming a perfect contrast to the tightly contracted scirrhus first described.

Squamous epithelioma is of rather frequent occurrence at the anus.

Parasites of the Intestine.—The great majority of the animal parasites spend at least a part of their life-history in the intestine. Thus, of the round-worms, the Ascaris lumbricoides, Oxyuris vermicularis, Trichocephalus dispar, Anguillula intestinalis and stercoralis, and Eustrongylus gigas; of the sucking worms, Uncinaria duodenalis; and of the tape-worms, Tænia solium, Tænia saginata, Bothriocephalus latus, and Tænia echinococcus, may be mentioned.

For the consideration of the life-history of these worms reference should be made to the section upon Parasites.

Hemorrhoids or **piles** are small tumors of the anal and rectal mucous membrane which are formed by vascular dilatation.

They occur in sedentary persons of constipated habit, and are about equally frequent in men and women. Heredity sometimes predisposes to them, but venous obstruction from cirrhosis of the liver, disease of the heart, frequent pregnancy, displacement of the pelvic organs, etc., are the chief causes.

Keen and White regard the erect position of the human body and the absence of valves from the hemorrhoidal veins as the chief predisposing causes of hemorrhoids.

They are clinically known as *external* and *internal hemorrhoids* according to their relation to the sphincter muscle.

According to their structure, they are divided into cutaneous, venous, columnar, and nevoid.

Cutaneous hemorrhoids consist of folds of the skin about the anus, which become pendulous and pedunculated through hyperplasia of connective tissue about the subjacent veins. They usually occasion no trouble, though they may become inflamed.

Venous hemorrhoids are dilated superficial veins which make their appearance just external to the sphincter muscle by a slight eversion of the mucous membrane. They often become large, hard, tense, and painful, and appear as bluish, rounded tumors. Ordinarily the blood can be expressed by pressure. Thrombosis not infrequently takes place in the tumor, which may become infected and suppurate or undergo organization.

Columnar hemorrhoids form within the sphincter. They are covered with the mucous membrane of the rectum, and are bright red in color, contain both venous and arterial vessels, and pulsate.

Nevoid hemorrhoids occur high up in the rectum as spongy-looking, rounded, bright-red tumors of small size. They are formed of both arteries and veins and bleed freely.

Further consideration of the subject will be found under Phlebectasia.

DISEASES OF THE LIVER.

Congenital Malformations of the Liver.—Congenital absence of the liver is very rare, and is seen only in acardiac monsters. Only one case is on record in which the liver was absent when the other digestive organs were present in anything approximating a perfect condition.

The congenital malformations of the liver are rarely of much importance. There may be too few or too many lobes; the lobes may be entirely separated from one another; the gall-bladder may be absent, and there may be accessory livers. The latter are usually detached fragments of hepatic tissue which have grown to perfection near by, but not joined to, the parent organ.

In cases of reversed viscera the liver may be upon the left instead of the right side of the abdomen.

Occasional rare cases of thoracic hernia of the liver are on record.

Acquired malformations of the liver are more frequent, that best known resulting from the pressure of the edge of the thoracic wall upon the liver as a result of "tight lacing." It causes a deep notch upon the anterior-superior surface of the organ. The hepatic tissue subjected to pressure has undergone atrophy and disappeared, leaving the fibrous tissue, which appears as a pale-colored band of almost tendinous consistence. The notch may be so deep as almost to divide the organ.

In rare cases an unusual relaxation of the ligaments of the liver gives it an abnormal degree of mobility, so that it may descend in the abdominal cavity and have its normal relations entirely changed. Such cases are more frequent in women than in men, and are described as "floating liver."

Anemia of the liver may occur in general anemia, or may depend upon ischemia from the pressure of neoplasms, displaced organs, etc. Swelling of the liver-cells may also produce anemia by closing contiguous capillaries. The anemic tissue is pale, and from the presence of small amounts of fat and bile-pigment may be yellowish or grayish-yellow. It may appear brownish in color when considerable pigmentation is present. When the anemic organ is incised, little or no blood escapes from the cut surface.

Hyperemia of the liver is very frequent both as a physiologic and pathologic process. Physiologic hyperemia is seen after meals. Pathologic hyperemia may be local, as in the neighborhood of areas of inflammation, etc., but it is usually a general process causing the entire organ to appear enlarged, slightly softened, and dark blue-red or brown-red in color. When incised, blood escapes from the tissue. It is seen in the course of the specific infectious diseases, in certain toxic conditions, and in the inflammatory diseases of the liver.

Passive hyperemia or chronic congestion of the liver depends upon inability of the blood to escape from the vena cava into the heart. It is to be expected in all cases of valvular heart disease, in all diseases interfering with the pulmonary circulation,—emphysema, chronic tuberculosis, etc.,—and in neoplasms pressing upon the vena cava.

The liver is enlarged and rich in blood in the early stages, and not infrequently shows the beautiful lobular mottling known as "*nutmeg liver*," in which the congestion of the central vein of the lobule contrasts with the paler surrounding zone.

If the condition persists for considerable time, the appearances change, because of atrophy of the parenchyma of the organ. The liver becomes uneven on the surface, more than normally resistant to the knife, shows a very marked nutmeg appearance of the cut surface, and has a paler color than before. It is spoken of as *cyanotic induration.*

When the tissue is examined microscopically, the central vein and its system of capillaries are found to be greatly dilated, full of blood, and the surrounding liver-cells in a condition of pressure-atrophy. So marked may the changes become that the entire capillary network of the lobule may be dilated and the entire parenchyma more or less atrophic. The atrophic cells are always most numerous in the center of the lobule. They have a shrunken, compressed appearance, and their protoplasm contains numerous yellowish or brownish pigment-granules in addition to globules of fat. In chronic cases many of the liver-cells are destroyed and their position indicated only by groups of pigment-granules.

The term *red atrophy* is applied to cases of passive congestion and atrophy with the deposition of pigment-granules resulting from blood destruction and the liberation of pigment.

The connective tissue of the liver rarely escapes proliferative changes, and about the portal vessels it is usual to find more or less round-cell infiltration and tissue hyperplasia.

Birch-Hirschfeld describes the naked-eye appearance of the nutmeg liver of passive congestion thus: "The described dilatation of the central vein and its adjacent capillaries produces a red central zone in the lobule; next comes a zone in which atrophic, pigmented liver-cells remaining between the dilated capillary vessels cause a brownish color; still further toward the periphery of the lobule is a pale-yellow zone of fatty degeneration of the liver-cells with bile stasis, upon which the thickened periportal connective tissue produces a delicate grayish covering."

Obstruction of the hepatic circulation by thrombosis, embolism, and endarteritis may be important according to the magnitude of the vessel obstructed. Thus, when the portal vein is closed by thrombosis, total cessation of bile secretion occurs, together with retention of blood in the portal system, and is frequently fatal.

The arterial anastomoses between the hepatic artery and the arteria coronaria ventriculi dextra, arteria gastroduodenalis, diaphragmatic, and other arteries are so perfect that arterial embolism may occur without important changes. That the liver is dependent upon the nourishment obtained from these vessels and cannot be supported by the portal blood alone has been proved by Cohnheim and others, who found that when all the arteries of the organ were tied, rapid necrosis resulted.

When life persists after portal thrombosis, the arteries of the liver are able to support its structure quite perfectly. There are, however, in these cases, necrotic areas, distributed more or less numerously throughout the organ, but these are usually dependent upon infectious emboli from the portal system rather than upon lack of nutriment.

Because of the rich anastomoses of the hepatic vessels, hemorrhagic and anemic infarctions are practically unknown in the liver.

Hemorrhage in the liver is seen in severe infections and in intoxications, also in purpura hæmorrhagica, and sometimes in thrombosis of the hepatic veins.

INFILTRATIONS AND DEGENERATIONS OF THE LIVER.

Pigmentation of the hepatic tissue is frequent as the result of—(1) Insufficient transformation of the blood-pigment into bile-pigment; (2) retention of the bile or excessive blood destruction, as in pernicious anemia and similar diseases, in which the destruction of blood corpuscles seems to liberate more pigment than the liver is able to destroy or transform; (3) it may also depend upon materials carried to the liver by the blood and deposited in its capillaries, etc., as in malaria and anthracosis.

1. Incomplete transformation of blood-pigment into biliary pigment is seen in nearly all forms of hepatic disease. It is rare in the normal liver. The condition is almost invariable in chronic congestion, amyloid disease, cirrhosis, and the cachectic conditions. The pigment occurs in the form of dark-brown, irregular-sized granules, which are found in the liver-cells, in the capillaries, and their surroundings. They are most numerous in the periportal zone and in the center of the lobule. When the granules occur in the liver-cells themselves, they usually occupy a position in their columns which suggests a distinct proximity to the fine capillary bile-ducts.

The pigment usually found is hemosiderin. It gives the blue color reaction with chemically pure sulphuric acid and ferrocyanid of potassium.

In pernicious anemia, etc., the iron containing granules are most numerous in the peripheral zone of the liver lobules.

2. *Retention of the biliary secretion* is associated with an impregnation of the liver-cells with the bile by which a dark yellowish-green or dark greenish-black color is imparted to them. In marked cases the pigment also collects in the form of concretions and irregular granular masses in the bile-capillaries. The biliary pigmentation is most marked in the central zone of the lobule.

3. The granules of melanin resulting from the blood destruction in malaria and the soot particles of anthracosis, when carried to the liver by the blood, are not retained in the liver-cells, but are collected in the walls of the capillaries, where they appear between the fibers of the periportal connective tissue.

Fatty infiltration of the liver is one of the most frequent changes. It occurs in normal individuals after hearty meals in which considerable fat has been taken, in healthy, overnourished individuals, in obesity, and in marasmatic individuals, chronic tuberculosis, and drunkards. In the former cases the infiltration probably signifies nothing more than that the metabolic functions have not yet succeeded in disposing of the excessive fat supply. In the latter case it probably indicates a profound error of nutrition, by which the fat which is abstracted from the tissues is retained in the liver pending its combustion.

The morbid anatomy of fatty infiltration is exceedingly simple. The liver is enlarged, sometimes to an enormous extent. It is yellow in color and is sometimes beautifully marked—"nutmeg liver"—by alternations of the fatty and normal tissue in each lobule. When the organ is incised, oil escapes and soils the knife and hands. The tissue is somewhat friable. When the cut surface is inspected, it may appear uniformly yellow when all the cells are infiltrated, or each lobule may be made conspicuous by a bright yellow periphery surrounding a darker normal or congested center.

Histology.—The fat is deposited within the liver-cells in the form of small droplets which soon coalesce and form larger droplets, which may become so large as to distend the cytoplasm into an attenuated surrounding envelope.

The nucleus is pushed aside, and is often compressed by the fat-drop, causing the cells to have the "seal-ring" appearance already described. The nucleus does not appear to suffer much, and there is little reason for thinking that except in extreme cases the function of the cell is much interfered with.

The infiltration begins in the peripheral zone of the lobule, near the periportal connective tissue, and spreads inward. It may affect only a narrow zone of cells or may involve every visible cell.

It is likely that fatty infiltration of the liver can readily recover. The fatty liver is apt to show some hematogenous pigmentation, which may indicate that its function of transforming hemoglobin into bilirubin is disturbed.

Fatty metamorphosis of the liver is less frequent. It is not always easy to differentiate from the fatty infiltration. It is found in some of the primary essential anemias,—pernicious anemia,—in various intoxications, such as phosphorus and arsenic, is seen in some of the severe infections (yellow fever), and gives its most typical picture in the peculiar and not clearly understood disease known as "*acute yellow atrophy of the liver.*" It is in this disease that the most extreme fatty metamorphosis of the liver is seen. It may, therefore, be taken as a type of the process, although it is not purely a disease of the liver, seeming to be an infectious or toxic affection with fatty destruction of various internal organs, the liver being the organ most seriously affected. The liver is much reduced in size, and thin and sharp at the edges. It may be but little larger than a man's hand. It is soft and flabby, and yields to pressure, like putty. It is yellow or ochre-colored, and rarely has the sulphur-yellow color of the fatty infiltrated liver. This is probably because icterus is a symptom of the disease, and biliary staining of the tissue is associated with it.

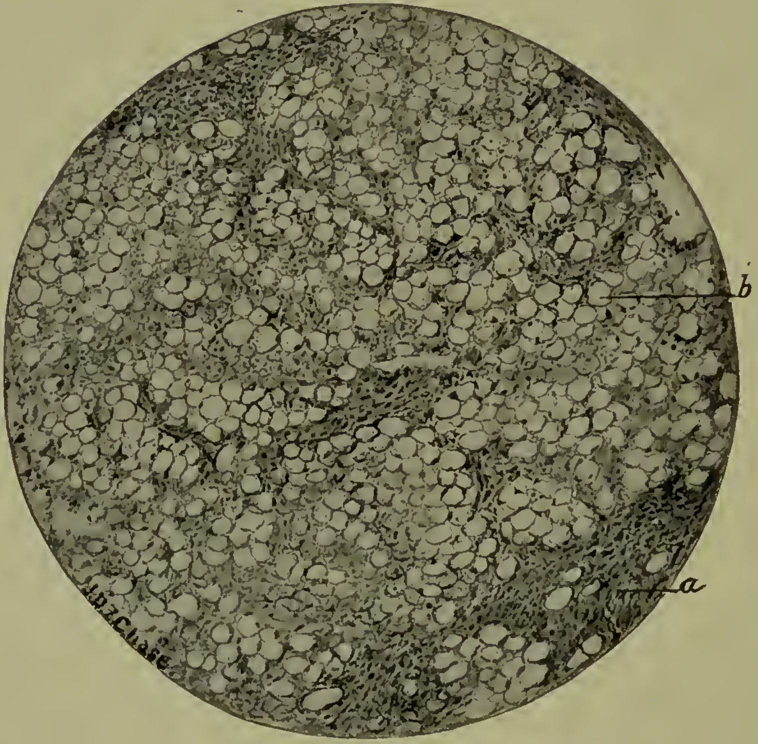

FIG. 257.—Fatty infiltration of the liver: *a*, Periportal connective tissue; *b*, fat-drops in liver-cells.

When the liver is incised, the yellow color is usually quite uniform, though it may be irregularly distributed in streaks. In some areas the liver tissue seems to have almost melted away, while in others it is firmer and has a more normal color. Because of their firmness the more normal areas seem to project from the cut surface. Oil runs out over the knife and fingers and drips from the specimen. It is easy to comprehend how fatty metamorphosis of the cells, the subsequent removal of the fat, and the consequent loss of substance all contribute to diminish the size of the liver.

When examined microscopically, most of the cells are found to be in a condition of advanced fatty metamorphosis. The cells contain small and large fat-droplets, which not infrequently coalesce to form larger drops, such as are seen in fatty infiltration. The outcome of the process is the complete destruction of the tissue. McPhedran and MacCallum, in a case that they studied, make special mention of an increase of the bile-capillaries. These little tubules became extremely conspicuous and were very numerous. It is not known whether they really proliferate or whether the destruction of the liver-cells and the subsequent condensation of tissue cause them to be more closely approximated and more readily seen than before. Numerous leukocytes invade the degenerated tissue and pick up the fatty molecules which are liberated.

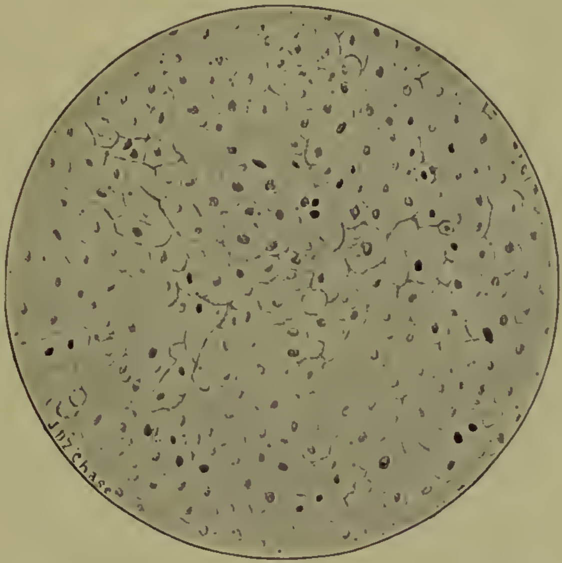

FIG. 258.—Fatty degeneration of the liver (taken from a case of phosphorus-poisoning). The cells are indistinct and are filled with small deposits of fat (Oc. 2; ob. 9).

The cause of acute yellow atrophy of the liver is unknown. Many regard it as infectious, Stroebe thinking that it depends upon bacteria of the colon group. Ziegler considers it, like arsenical and phosphorus poisonings, to depend upon some poison absorbed from the intestine.

The disease has been observed more frequently in women than in men. It has been seen after infectious diseases and after traumatic or puerperal sepsis and syphilis. It may, however, develop suddenly in healthy persons.

The degenerative process seems to occur first in the peripheral zone of the lobule and spread toward the center. This would be in favor of the etiologic agent entering with the portal blood.

In some cases the shrunken atrophic liver after death is found to be much congested, and is spoken of as *red atrophy* instead of as yellow atrophy.

The disease is nearly always rapidly fatal. When death is delayed, it is found that there are remnants of normal tissue, seemingly uninvolved in the process, which were able for a time to continue a compensatory function. If the patient recovers, the liver subsequently presents a peculiar appearance, the normal tissue alternating with the depressed destroyed areas, giving the organ a nodular, irregular appearance easily mistaken for cirrhosis.

The fatty livers of *phosphorus* and *arsenical* poisonings closely resemble those of acute yellow atrophy.

. The liver of *yellow fever* is characterized by a "box-wood" color and appearance. It may, however, be dark or even brownish in color. It is invariably fatty degenerated and necrotic. According to Birch-Hirschfeld, the changes in the liver are essentially identical with those of acute yellow atrophy in its early stages.

Amyloid Disease of the Liver.—Amyloid disease of the liver occurs in tuberculosis, chronic suppurations, decubitus, etc.

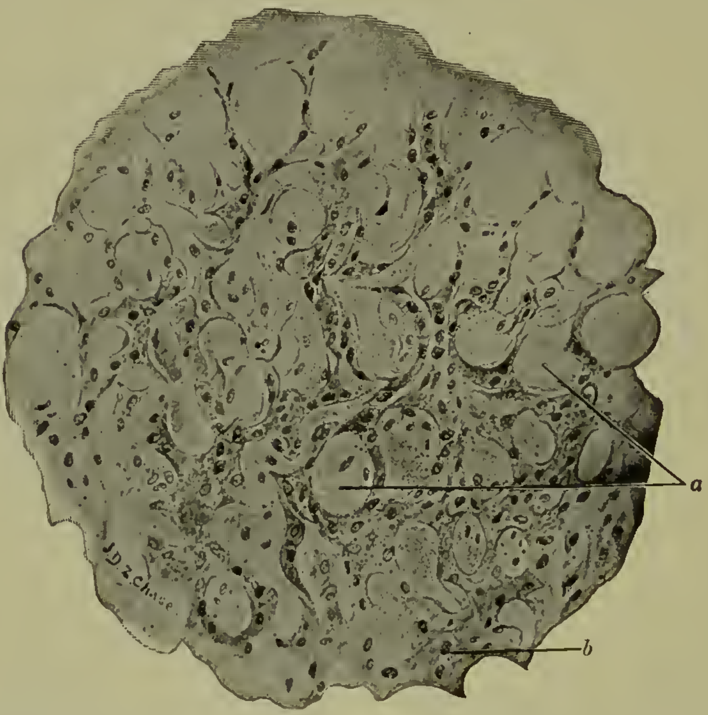

FIG. 259.—Amyloid degeneration of the liver: *a*, Amyloid masses; *b*, liver-cells (Oc. 2; ob. 9).

The liver is enlarged, and in extreme cases may be of enormous size. It is unchanged in color, and has a smooth surface, with rounded edges. There is a peculiar and characteristic translucency about the tissue, which is less elastic than normal and remains pitted when pressed with the finger. The cut surface has a peculiar glassy appearance, and the tissue seems to be unusually homogeneous.

In doubtful cases the application of Lugol's solution to a thin slice of the tissue should develop the characteristic color.

When studied microscopically, the disease is seen to occur first in the peripheral and intermediate zones of the lobules. The walls of the capillaries, which are first affected, appear to contain amyloid masses which destroy the endothelium, and by internal projection obstruct the vessel, and by outward projection press upon and compromise the vitality of the liver-cells, many of which disappear by atrophy. The amyloid process continues its invasion along the capillaries and intermediate connective tissue until large homogeneous areas are formed. In and between these a few atrophic liver-cells are seen here and there. The liver-cells are functional as long as they are not destroyed by atrophy, so that the function of the amyloid liver is retained until quite late. All grades of the disease are seen.

Fatty infiltration, pigmentation, and bile stasis occasionally occur with amyloid. In cases of combined advanced fatty and amyloid liver the organ may appear mottled, with alternating gray and yellow patches.

Parenchymatous Degeneration of the Liver.—*Cloudy swelling*, or *parenchymatous degeneration of the liver*, is seen in most of the infectious diseases and in various intoxications. It is spoken of by some writers as *acute parenchymatous inflammation* of the organ. The changes are simple. To the naked eye the liver is slightly increased in size and somewhat congested. It may appear anemic if the cells are much swollen, and then has a grayish color instead of the normal dark red. The tissue feels somewhat elastic, but when cut, is soft and lacerable.

When examined microscopically, the cells present the characteristic granular appearances of cloudy swelling.

The regularity with which parenchymatous degeneration of the liver accompanies the infectious diseases suggests that it readily recovers when the cause is removed.

Glycogenic Infiltration of the Liver.—This condition occurs in diabetes and other forms of glycohemia. The glycogen is present as clear drops in the liver-cells, chiefly in those of the peripheral zone of the lobule. It cannot be recognized with the naked eye, but can be demonstrated microscopically by the use of the proper reagents (glycogenic infiltration) in tissues that have been properly preserved. It can be mistaken for fatty infiltration in badly prepared specimens.

Atrophy of the Liver.—Atrophy of the liver is a rare primary condition which depends upon local anemia or marasmus. As a secondary condition it is quite frequent, and may depend upon internal or external causes, which, however, nearly all operate through pressure. Thus, the pressure exerted upon the liver by the margin of the costal cartilages in tight lacing, the contracting cicatricial bands in cirrhosis, etc., all press upon the parenchyma of the organ and cause its atrophy. In amyloid disease it is pressure upon the liver-cells, combined with malnutrition, that brings about atrophy of the parenchyma.

The result of atrophy is diminution in size. The organ may be but one-half its normal size.

The atrophic cells, when examined microscopically, appear flattened, attenuated, granular, and pigmented. Occasionally they contain fatty granules. The nucleus is retained for a time, but finally disappears with the formation of distributed chromatin granules.

The hepatic tissue also has a tendency to undergo simple atrophy in old age.

Hypertrophy of the whole liver probably does not occur. Compensatory hypertrophy of certain parts may occur in consequence of various pathologic processes.

Leukemic Infiltration of the Liver.—In leukemia the liver is subject to an invasion of leukocytes which leave the blood vessels and seem to proliferate in the tissue. The leukocytes abound in the periportal connective tissue, and sometimes also occur in considerable numbers near the center of the lobule. The distribution of the cells is too regular and uniform to be mistaken for infection.

INFLAMMATION OF THE LIVER.

The **acute interstitial inflammation** of the liver depends upon the presence of micro-organisms in the hepatic tissue. Nearly all the hepatic inflammations are secondary to diseases of the stomach, intestines, heart, etc. They are always suppurative in character, and the extent and duration of the process are always in keeping with the nature of the infection.

According to Schmaus, there are five avenues by which bacteria may enter the liver:

1. *The Portal Vein.*—In all cases of ulcerative diseases of the stomach and intestine with tissue denudation it is possible for bacteria to enter the portal vein and be carried to the liver.

2. *The Hepatic Artery.*—This vessel is rarely the cause of septic infection, but there are cases of malignant endocarditis in which embolism of this artery is known to lead to abscess of the liver.

3. The *hepatic veins* are sometimes the collecting place of micro-organisms which are able to pass through the capillaries, but which remain in the veins, causing hepatophlebitis, and sometimes thrombosis of the vena cava. The extension of the phlebitis to the smaller vessels is followed by suppuration.

4. The *umbilical vein* of newly born infants is an avenue of entrance along which bacteria can pass to the liver.

5. The *bile-ducts* are not infrequently invaded by bacteria, which lead to obstruction, ulceration, calculus formation, etc.

No matter how pyogenic bacteria reach the liver, they sooner or later cause suppuration. There may be a single or several large abscesses, or there may be innumerable minute abscesses, some of which are discoverable only with the aid of a microscope.

The micro-organismal emboli lodging within the capillaries originate in the foci of suppuration.

In thrombophlebitis or pylephlebitis the diseased areas correspond to the course and distribution of the respective vessels, and may be traced through the liver tissue with the naked eye, as softened, creamy lines of suppuration. When due to portal or hepatic embolism, the abscesses develop from one or several foci, and may become so large that the entire organ is threatened with disorganization. When resulting from dysentery, multitudes of minute miliary suppurative points may be found scattered throughout the organ.

The small abscesses terminate in complete recovery by absorption unless their number be so great as to cause death by interrupting the hepatic function. Larger abscesses, in which considerable tissue is destroyed, may rupture with fatal peritonitis or rupture into the pleura, causing empyema, or into the lung, or they may slowly cicatrize after isolation by walls of granulation tissue.

The diseases to which liver abscesses are secondary are themselves not infrequently fatal. The patient with a large hepatic abscess is still in danger, however, lest the abscess, by rupture and evacuation, compromise life. The evacuation may occur into the abdominal cavity or externally. Adhesions may form between the liver and diaphragm and others between the lung and pleura; when this happens, it is possible for the abscess to rupture into the pleura or into the lung, so as to evacuate through the bronchial tubes, and that liver-cells still in a recognizable condition may be found in the expectorated pus.

A single large abscess—tropical abscess of the liver—seems to be caused by the Amœba coli, which enters the liver during dysentery. It may be, however, that they are caused by bacteria that enter with or independently of the ameba. These abscesses may involve nearly the entire organ. They usually occur in the right lobe. The pus which they contain is of a grayish or pinkish color, and of a gummy consistence, quite unlike ordinary pus. The walls of the abscess are thick and necrotic.

Chronic Interstitial Hepatitis or Cirrhosis of the Liver.—Cirrhosis is a common disease of the liver characterized by hyperplasia of the connective tissue, chiefly in the periportal region, which develops in the form of bands and septa which, by gradual contraction, lead to atrophy cf the organ.

Etiology.—The etiology of the disease is in doubt. It is apparently the result of prolonged mild irritation of the tissue elements contiguous to the portal vessels by some irritant conveyed to them in the blood of the portal vein. The most frequent of these seems to be alcohol. Cirrhosis of the liver is most common in those countries and among those peoples where the use of concentrated alcoholic stimulants prevails ("Säuferleber" of the Germans).

Syphilis is a frequent cause of the affection, but the cirrhosis of syphilis differs from the ordinary form.

Gout and kindred affections are put down as causes, but, as Eichhorst suggests, they are usually associated with alcoholism, and it is difficult to eliminate the effect of alcohol in the etiology of the disease.

Malaria seems to be an occasional cause of cirrhosis of the liver, especially in Italy, where the matter was investigated by Catani and Franco. Of 36 cases studied by von Frerichs, 14 per cent. seemed to depend upon malaria.

Kline observed proliferative changes in the livers of children dying of scarlatina. Osler points out that infectious diseases may have a distinct bearing upon the cases of cirrhosis of the liver in childhood. It has also been noted after typhoid fever.

Rickets is said sometimes to be a cause. Anthracosis causes connective-tissue proliferation in the liver as well as in other organs.

Biliary obstruction also causes a well-characterized form of the disease.

A toxic cirrhosis resulting from phosphorus poisoning has been described by Eichhart, Wegener, and others.

Obstruction of the portal vein is said by Botkin and Solowieff to occasion changes identical with cirrhosis, but as cirrhosis sometimes causes thrombosis of the portal vein, one must be cautious about accepting this as a cause.

Senile atrophy of the parenchyma also occasionally produces a condition resembling cirrhosis. Many cases occur without discoverable causes.

An interesting statistical study of cirrhosis of the liver was made in Berlin by Forster. Of 3200 necropsies, the disease was discovered 31 times. Of these, 24 were in men and 7 in women. Between the first and twentieth years of life, 1 case; between thirty and forty years, 4 cases; forty and fifty years, 10 cases; fifty and sixty years, 6 cases; sixty and seventy years, 4 cases; and between the seventieth and eightieth years, 1 case, were noted.

Morbid Anatomy.—Pathologically, the disease is characterized by proliferation of the connective tissue of the liver, contraction and atrophy of its cells, more or less round-cell infiltration of the interstitial tissue, and proliferation of the bile-ducts. Frequently there are associated pigmentation and fatty infiltration. Two forms of the disease are described: the usual form, which may be characterized as *hematogenous*, and a rare form, which follows biliary stasis, *hepatogenous*. The first form is supposed to depend upon irritating substances, alcohol, ptomains, leukomains, etc., brought to the liver by the blood of the portal system; the second form, depending upon the irritating effects of retained bile.

The *hematogenous cirrhosis* may also be characterized as—(1) atrophic; (2) hypertrophic.

These two forms are quite distinct in macroscopy and microscopy, and are not different stages of the same process, as will be made clear by the descriptions which follow:

1. **Atrophic Cirrhosis of the Liver (Chronic Interstitial Hepatitis; Drunkard's Liver; Säuferleber; Laennec's Cirrhosis).**—The macroscopic appearance of the organ is strikingly characteristic. It is reduced in size according to the extent and duration of the disease, and may be only two-thirds its natural size, and weigh only 700 to 900 grams. The edges of the organ are thin and sharp. The surface is extremely irregular, and presents large numbers of rounded, projecting nodules of smooth, dark-colored, soft liver tissue, alternating with tough gray bands of surrounding cicatricial tissue. The surface will vary considerably in appearance according to the distribution of the connective tissue. When uniformly distributed throughout the liver, the surface of the organ is granular. When less regularly distributed, so that the connective-tissue bundles are larger and surround groups of lobules instead of single lobules, the surface is more irregular and justifies

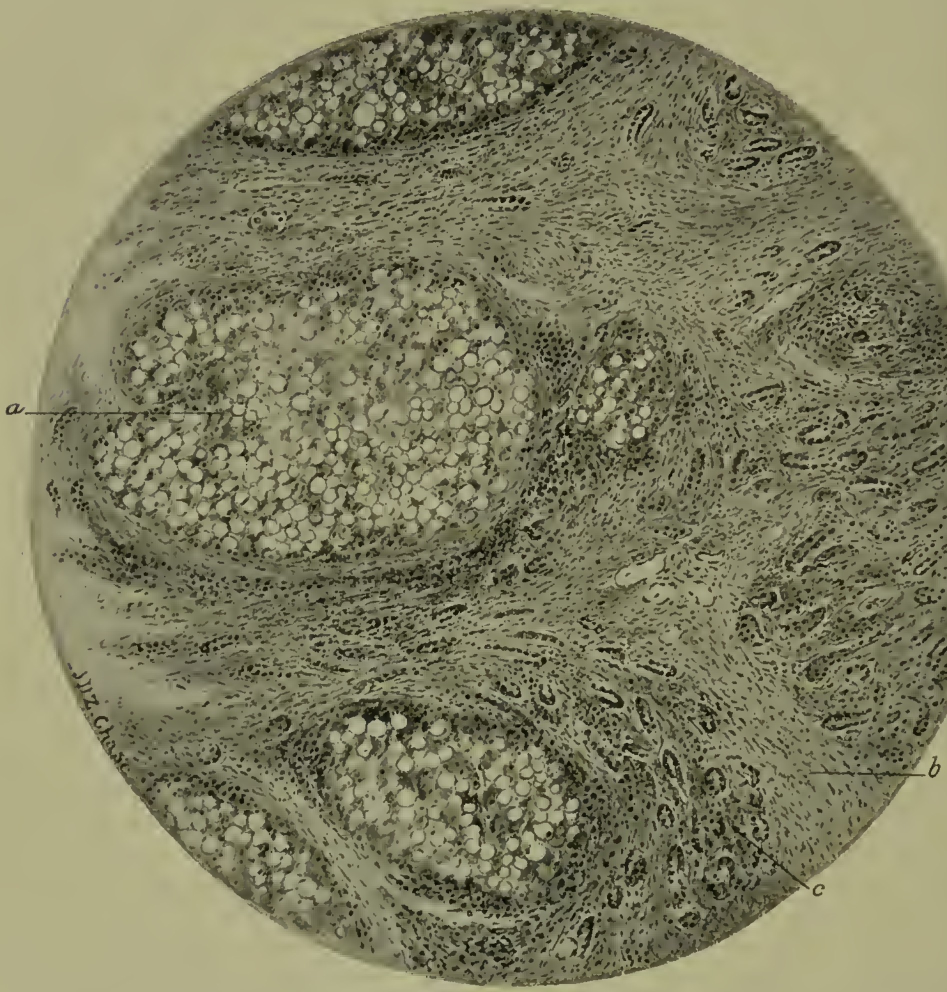

FIG. 260.—Chronic indurating cirrhosis of the liver: *a*, Liver lobule, most of whose cells are in a fatty infiltrated condition; *b*, greatly hypertrophied periportal connective tissue; *c*, proliferated bile-ducts.

the common appellation, "*hob-nail liver*," the surface being covered with coarse irregularities. In the extreme form, and especially in the syphilitic cirrhosis, the liver is divided by deep fissures corresponding to dense, firmly contracted cicatricial bands of connective tissue.

The "hob-nail" liver is the common form. The organ is frequently stained with bile, and sometimes presents a really beautiful appearance, depending upon the variegated effect of alternating dark cellular areas and pale yellowish-green connective tissue. The normal areas seem to be under pressure and project from the organ with bright polished surfaces and translucent qualities that sometimes cause the novice to mistake them for cysts.

When incised, the cut surface shows the entire hepatic substance divided by connective tissue into innumerable small areas, usually of pin-head size, though sometimes much larger. This gives the organ a nutmeg appearance. The substance is firm and hard, and the knife creaks as it cuts into the indurated tissue. The capsule is sometimes thickened and opaque.

Histology.—The disease seems to begin with a limited leukocytic infiltration of the periportal connective tissue. Occasional epithelioid cells and fibroblasts are present. Little by little fibers of connective tissue are added to those of the periportal tissue, and in the course of time the lobules become outlined by fibroconnective-tissue bands. Along the lines of the sublobular veins the deposition of fibers is more marked and thicker cicatricial bands are formed. Sometimes the connective tissue is sparsely infiltrated with small round-cells. As the tissue becomes fully formed, these disappear and the tissue is cicatricial in character.

As the bands of connective tissue contract, pressure is exerted upon the parenchyma, and the liver-cells atrophy. The atrophy is shown by attenuation of the cells pressed upon and the occurrence of granules of pigment and fat within them. Through the atrophy of its cells the parenchyma becomes reduced in amount, and the size of each lobule diminished.

The liver-cells not subjected to the pressure of the connective-tissue bands may appear normal, may be infiltrated with bile, or, as is much more common, may be the seat of fatty infiltration. Indeed, fatty infiltration is very frequent in association with cirrhosis, and livers are not infrequent in which scarcely a single cell escapes.

In the relations of the cells to one another, and of the columns of cells to each other, the lobules are usually quite normal, the entire lobule being surrounded by the connective tissue. Sometimes, however, in the atrophic form, there is a partial invasion of the cellular tissue by processes of connective tissue which isolate groups or columns of cells. Such detached cells, pressed upon all sides by the fibrous elements, soon fall into an atrophic condition, lose their normal appearance, and may be mistaken for bile-ducts, as Schmaus points out.

The bile-ducts are peculiarly affected in cirrhosis of the liver. In some cases no change can be observed, but, as a rule, the bile-ducts appear distinctly more numerous than normal, and in some cases so many small bile-ducts may be present in the newly formed connective tissue as to suggest tubular adenoma.

Upon what condition these changes in the bile-ducts depend is not clear. Some may have preëxisted and become conspicuous by the loss of hepatic cells; some may be composed of isolated and atrophic columns of liver-cells, as Schmaus suggests; but every one who studies extreme cases must admit that the bile capillaries are more numerous than could possibly have been normal.

The interpretation usually placed upon the increase in the biliary ducts is that it is an effort at regeneration, and that, as atrophy is taking place in certain of the parenchymatous elements, the outgrowth of the bile-ducts is compensatory and preliminary to new liver-cell formation.

The induration and contraction of the liver in cirrhosis cause marked disturbance of the abdominal circulation, obstructing the passage of the blood through the portal vein, and necessitating the establishment of a compensatory collateral circulation through various of the anastomosing veins. Of these, may be mentioned the veins which pass through the round and suspensory ligaments of the liver, uniting the portal system with the epigastric and mammary veins, branches in the neighborhood of the gall-bladder and suspensory ligament which connect with the diaphragmatic veins and finally enter the vena azygos. Anastomoses also occur with the gastric and esophageal veins and with the hemorrhoidal and inferior mesenteric veins. The veins of Retzius must also be mentioned as uniting the portal branches in the intestines and mesentery with the inferior vena cava.

Although the contraction and vascular obliteration in the liver must progress slowly and thus enable the veins gradually to enlarge and carry off the blood, the collateral circulation thus established is never sufficient, and patients with cirrhosis always suffer from ascites, hemorrhoids, and other conditions indicative of venous obstruction.

The biliary secretion is not profoundly affected, and in most cases jaundice is not a symptom of the disease. There may, however, be local or universal biliary stasis, with marked pigmentation of the tissues.

The hepatic cells in cirrhosis sometimes escape compression, even when much connective tissue is present. Their atrophy may in many cases depend in part upon irritating substances brought to the liver by the portal blood. The position of the atrophic cells is nearly always at the periphery of the lobule, where this would be possible, but where, too, the effect of compression would be most marked.

While the portal vessels are compressed and obliterated by the cirrhotic changes, there seems to be proliferation of the arterial vessels. When attempts are made to inject the cirrhotic liver through the portal vein, they usually fail, but attempts to inject it *via* the hepatic artery usually succeed well.

Pigmentation of the liver-cells with yellowish, yellowish-green, or olive granules deposited in the newly formed connective tissue, within the hepatic cells, Kupffer's cells, and the endothelium of the vessels, is frequent. The pigment may be hemosiderin, which is sometimes present in large quantities, or may be bile-pigment, which is usually found in the hepatic cells and rarely in the connective tissue.

II. **Hypertrophic Cirrhosis (Hanot's Cirrhosis).**—This is also called by French writers *cirrhose biliaire hypertrophique*. Hypertrophic cirrhosis of the liver is characterized by a marked increase in the size of the organ, which, in well-marked cases, may weigh as much as 4000 grams. The surface is either smooth or finely granular, with minute rounded eminences; its edges are rounded, its substance, dense and firm. When incised, it gives less of the creaking sensation than is observed in the atrophic form. Upon the cut surface a peculiar variegated, mosaic-like marking is observed, which depends upon alternating pale gray, dull yellow, and greenish spots. There is no sharp circumscription of the lobules by connective tissue, as is seen in the atrophic form, but one observes that the grayish connective tissue occurs in irregularly distributed islets and processes.

There are no signs of contraction of the connective tissue, the portal circulation seems not to be affected, and it is said that specimens injected through the portal vein show all the finer vessels patulous.

The dark-greenish color, which is so marked in hypertrophic cirrhosis, is also different from that seen in the atrophic cirrhosis, and depends upon bile stasis, which, it will remembered, is unusual in the atrophic form. In his investigations Charcot found that there was usually a characteristic periangiocholitis of the interlobular bile-ducts.

Microscopically, one observes that the interlobular bile-ducts are obstructed by pigmented masses of degenerated products and their walls surrounded by fibroconnective tissue. There are also numerous normal interlobular bile-ducts, some of which are in active proliferation. There is considerable newly formed connective tissue, which, however, is not deposited between the lobules, as was the case in the atrophic form, but which extends into the lobules, between the columns of liver-cells. This topographic arrangement, by which the connective tissue, instead of circumscribing the lobules of the liver, occurs in islets and intralobular processes, is quite characteristic of the hypertrophic form of the disease. The connective tissue may be increased throughout all parts of the lobule, and the liver-cells and columns of cells separated by it.

The liver-cells are injured both by the retained and altered bile and by the pressure of the connective tissue, and while showing little alteration in ordinary cases, may be completely destroyed and represented only by masses of pigment granules in severe fatal cases of the disease. When the progress of the disease is slow, one finds a marked proliferation of bile-ducts, which may be interpreted as a regenerative effort. The most marked proliferation of bile-ducts occurs in hypertrophic cirrhosis of the liver. Because of this marked increase of the bile-ducts the condition may closely suggest adenoma. Cystic dilatation of the bile-ducts is not infrequent, and has been called by Sabourin *angiome biliaire kystique.*

Birch-Hirschfeld points out that the growth of bile-ducts is on the border-line between the typical and atypical epithelial growths, and closely resembles other conditions observed in the hepatic tissue the seat of a neoplasm.

While the hypertrophic cirrhosis is thus characterized in typical cases, it is sometimes impossible to separate the hypertrophic and atrophic forms etiologically, and between typical cases of both are many cases bearing distinct resemblances to each. So true is this that the French authors have styled the intermediate forms "*cirrhoses mixtes,*" in order to overcome the difficulty. Whether or not the two conditions are really different processes, or whether they are different manifestations of the same process modified by accidental conditions, is not known at present.

III. **Biliary hepatitis** or **biliary cirrhosis of the liver** is a name frequently applied to a cirrhotic condition which follows obstruction of the large bile-ducts by calculi, etc. The bile stasis which results from the obstruction is a cause of marked irritation, but usually has added to it an infectious element caused by the entrance of bacteria from the intestine into the bile. Bile stasis alone is insufficient to bring about the inflammation, and in cases of tumor or other conditions associated with complete permanent obstruction of the bile ducts, biliary cirrhosis does not occur. It is most frequent in cases of impacted gall-stones either in the hepatic ducts or in the ductus choledochus near its entrance into the wall of the duodenum.

The irritating effects of the stagnated bile is exerted upon peripheral parts of the lobules, where small necrotic areas are sometimes observed. This necrosis and irritation are succeeded by hyperemia and round-cell infiltration of the perilobular connective tissue, which progress to actual abscess formation in cases where bacteria are actively at work in the bile-ducts, or may simply precede the formation of additional fibers of connective tissue.

Ziegler divides the biliary cirrhosis into two forms—the *suppurative* and the *indurative,* according to the predominance of one or the other process. The cirrhotic or indurative form resembles the hypertrophic cirrhosis in its general characteristics.

Proliferation of the bile-ducts also occurs in this form of hepatitis, and progresses, together with connective-tissue formation, as the liver-cells are injured and undergo atrophy and degeneration. Regeneration of destroyed liver-cells is also attempted, as is shown by karyokinetic figures.

The liver of biliary cirrhosis is increased in size in the early stages, but soon, because of the contraction of the cicatricial tissue, becomes small. The hepatic tissue has a homogeneous, dark-green color.

The infection, if terminating in abscess formation, may be associated with hectic temperature—" *Charcot's hectic.*"

Syphilis of the Liver.—Adults with acquired syphilis may suffer from a diffuse proliferation of the connective tissue, accompanied by contraction and atrophy of the parenchyma closely resembling atrophic cirrhosis. More usually the syphilitic cirrhosis is characterized by more marked and more circumscribed connective-tissue formation, in which great bands of dense fibrous tissue separate the organ into many small lobes, each of which is rounded and well defined.

In other cases the acquired disease is characterized by *gumma* formation. The gummata may be single or multiple. Single gummata may be as large as the fist; multiple gummata are usually smaller.

They are readily recognized by the coagulation-necrotic contents, the granulation tissue surrounding them, their gray or grayish-yellow color, and their tendency to heal with radiating cicatrices which cause deep puckers or fissures in the organ. These may entirely transform the appearance of the liver by altering the lobar arrangement. Occasionally one finds gummata in all stages of development in the same liver.

Congenital syphilis of the liver is still more varied. In some cases a dense fibroid induration is observed, by which the organ is increased in size and made hard and firm. Its quality has been compared by Trousseau to sole leather. The color of the organ is yellowish, varying to dark brown, and it is sometimes spotted. Upon the surface, careful inspection or examination with a hand-lens reveals small yellowish-white spots or stripes which correspond to the connective-tissue bundles. When examined microscopically, a wide-spread hyperplasia of the connective tissue, with numerous round-cell infiltrations, is observed. The round-cell infiltrations are apt to occur in the neighborhood of, and in the walls of, the blood vessels, sometimes extending to the endothelium. The distribution of the connective tissue is in general much like that seen in hypertrophic cirrhosis.

The liver-cells may be well preserved, but are more apt to fall into fatty degeneration. The condition is sometimes described as "acute yellow atrophy" of the liver of the new-born.

In congenital syphilis miliary gummata may also be seen. They appear as grayish or yellowish-white dots, about the size of a pin-head, evenly distributed throughout the liver substance. They are never sharply circumscribed. When irregular in size, the larger ones may have a yellow center with grayish surroundings. The larger nodules are chiefly interlobular in position, and may occupy the wall of a blood vessel or bile-duct. The smaller nodules occur irregularly. Microscopically, the miliary gummata present the usual appearances and exhibit cheesy centers with granulation tissue in the periphery.

Larger gummata, such as are seen in acquired syphilis, are rare in the congenital form. A peculiar gumma of the liver sometimes occurs at the hilus of the organ in new-born infants, and invades the portal vein and bile-ducts. In healing it forms an enormous branched cicatrix extending from the hilus into the liver tissue, obstructing the portal vein and occasionally occluding the bile-duct.

Ziegler describes two forms of diffuse congenital syphilitic changes in the liver: first, a diffuse connective-tissue change extending over the entire organ, inter-acinose and intra-acinose, accompanied by cellular accumulations or marked connective-tissue proliferation. The liver is usually dark red. Only when the areas of cellular infiltration are large can they be recognized by their gray color.

In the second form the connective-tissue proliferation is easily recognized by the fawn-yellow color, the absence of lobular differentiation on the cut surface, and the density of the tissue.

There may be inflammatory exudates upon the surface of syphilitic livers or they may adhere to adjacent organs.

Tuberculosis of the liver may be of hematogenous or lymphogenous origin. It usually occurs in the form of miliary tubercles, irregularly scattered throughout the organ, and requiring no special description. They are usually secondary to tuberculosis of the lung, and form part of general miliary tuberculosis. The tubercles are seen with the naked eye with great difficulty, and in many cases entirely escape observation until microscopic examination of the organ is made. The microscopic appearances of the tubercles are typical. When the lesion is very acute, numerous small punctiform hemorrhages may at times be seen. Tuberculosis of other abdominal organs may cause secondary tuberculosis of the liver by lymphogenous distribution.

Primary tuberculosis of the liver is a rare affection. It is thought by some that it is always congenital and caused by the entrance of bacilli into the liver through the umbilical vein during fetal life. This is, however, scarcely probable. There may be a single or several large cheesy masses, varying in size from a hazelnut to an egg.

Tuberculous hepatitis is a name used to describe a rare form of tuberculosis of the liver associated with connective-tissue proliferation. The parenchyma is more or less divided up by bands of connective tissue in which larger or smaller cheesy nodules occur.

Lepra of the liver is characterized by the occurrence of the specific granulomatous lesions, in which the characteristic large cells are filled with the lepra bacilli. The lepra nodules are very rarely found in the liver.

Actinomycosis of the liver is of rare occurrence. The usual communicating suppurating cavities and sinuses are seen. There is always considerable inflammatory disturbance about the seat of disease, and perihepatitis with adhesion to adjoining parts is usual.

The disease is usually secondary to actinomycosis of the lung, the liver becoming invaded through the diaphragm.

TUMORS OF THE LIVER.

Angioma is one of the most frequent tumors of the liver. It occurs in the form of small, single or multiple, more or less circumscribed, dark-red, purplish, or bluish spots upon the surface, which, upon incision, are found to descend to a depth about equal to their diameters into the subjacent tissue. Upon microscopic examination the tumor is found, in most cases, to be a cavernous angioma, although racemose angioma occasionally occurs. The tumors vary in size from a pin-head to a man's fist. They do not increase the size of the organ, nor do they injure any part of it beyond the area of their own growth. The substance of the tumor is spongy. The tumor occurs most frequently in the aged and in the badly nourished. It probably develops by dilatation of certain capillary systems. The intermediate liver-cells disappear by atrophy.

Fibroma rarely occurs. It is seen chiefly in the form of disseminated nodules, and is most frequent in *neurofibroma molluscum*.

Lipoma is rarely seen in the liver, and is of no clinical importance.

Sarcoma may be primary or secondary, the latter form being the more frequent.

The **primary sarcoma** develops from the connective tissue of the hilus, the periportal areas, or from the tissue of the blood vessels or biliary ducts. The tumor is usually found in the neighborhood of a blood vessel. There may be but one node or the liver may be studded with them. Multiplicity of the lesions, however, usually indicates that the growth is secondary. The tumor may be composed of round- or spindle-cells, and gives metastasis to other organs.

Secondary sarcoma is of hematogenous origin, and is characterized by the formation of multiple, larger or smaller, disseminated nodules, which are not, as a rule, sharply circumscribed. The tumor tissue may fade away gradually into the liver tissue occupying the spaces between the cells, filling the capillaries, and slowly leading to atrophy of the liver-cells.

Occasionally the sarcoma nodules are quite well circumscribed. The tumor consists of cells, either round or spindle in shape. Melanotic secondary sarcoma is frequent in the liver. The presence of sarcoma, either primary or secondary, causes the liver to become increased in size. The tumor nodes form larger or smaller, more or less rounded masses of pale color, except when vascular, which may be superficial and project from the surface, or deep in the liver tissue.

Adenoma of the liver is rare. It occurs in otherwise normal livers and sometimes in cirrhosis. The tumor appears in the form of solitary or multiple, grayish or yellowish-white, occasionally reddish or brownish nodes, varying in size. They may be as large as an egg. They are encapsulated by connective tissue.

When examined microscopically, they consist of elements which resemble bile-ducts and from which they probably develop. In some cases columns of liver-cells entirely lacking the usual lobular arrangement are thickly distributed among the bile-ducts. The adenoma is benign, though it possibly, at times, becomes malignant. The adenoma not infrequently becomes cystic—this form of tumor being described as *adenocystoma* of the liver.

Carcinoma of the liver may be primary or secondary.

Primary Carcinoma of the Liver.—This tumor presents itself in a variety of different forms. Three of them are well characterized: (1) More or less circumscribed massive tumor nodes; (2) diffuse carcinomatous infiltration with general enlargement of the liver; (3) an interlobular carcinomatous development which probably originates from the bile-ducts.

1. The *circumscribed nodular growths* usually occur in the right lobe of the liver, and appear as well-circumscribed, grayish-yellow nodes of various size, sometimes as large as the fist. The nodes may be single or, more rarely, multiple. The central part of the node is usually firm and fibrous, but may be soft and degenerated. The nodes are not distinctly encapsulated, though not infrequently one finds part of the growth well circumscribed by connective tissue.

There is usually, however, some part of the tumor that gradually invades the surrounding tissue. This partial encapsulation of the nodes, their general appearance, and not a few of the histologic appearances, are highly suggestive of original development from adenomata. Indeed, Wulff and Hansemann have investigated the subject, and have shown every intermediate step between the benign and malignant tumor.

Microscopically, the growths are made up of irregular cell-nests distributed throughout a fibroconnective-tissue reticulum. The appearance of the cells suggests that they were originally derived from the liver parenchyma, but in the course of rapid growth they seem to have become smaller and developed a greater affinity for the stain, thus appearing more like the cells of the bile-ducts. Fatty degeneration of the cancer-cells is common in the carcinoma nodules. Necrosis of the cells may also occur, and hemorrhages are not infrequent. When carcinoma nodules are superficial, whether they are primary or secondary, they are usually characterized by a *central umbilication* depending upon degeneration, absorption, and collapse of the tumor masses. The liver containing the carcinoma nodes is always enlarged.

The primary tumors are occasionally pigmented—*melanocarcinoma*.

2. *Diffuse carcinomatous infiltration* with general increase in the size of the liver is very peculiar. To the naked eye, the liver is considerably enlarged and presents an irregular granular and nodular surface, like that seen in cirrhosis. Here and there considerable sized masses, which seem to be more or less circumscribed, are present.

When incised, the organ has a peculiar appearance, its normal color having given place to a grayish or brownish tint. No normal liver tissue may be found. Except for the occasional undoubted cancer nodes, the entire organ presents a more or less similar appearance.

When studied microscopically, it becomes apparent that the entire liver is infiltrated with carcinoma cells, the original lobules being separated by cicatricial bundles, as in cirrhosis. Between these bundles, in what represent the lobules of the liver, inconspicuous atrophic liver-cells are being crowded out of existence by robust carcinoma cells. The development of the tumor seems to depend upon the distribution of the abnormal cells by the blood. The cancer-cells occupy the capillaries, in which they grow luxuriantly and exert pressure upon the exterior liver-cells. Where large collections of the cells occupy a good-sized vessel, in which they grow rapidly, nodes are formed, which, like those of the primary focus from which the disease originated, can be recognized by macroscopic examination.

The tumor growth entirely destroys the function of the liver, and obliterates both its blood vessels and its bile-ducts.

3. *The Interlobular Carcinoma Following the Distribution of the Portal Vein.*—In this form the liver is invaded by numerous whitish or grayish nodes, which distribute along the course of the interlobular circulation and invade the neighboring tissue by extension. The carcinomatous tissue is fairly well differentiated from the healthy tissue of the liver lobule. To the naked eye this form presents some of the appearances of the cirrhotic liver, the surface being marked by similar alternating tumor nodules, atrophic areas, and cicatricial bands.

Secondary carcinoma of the liver is frequent is cases of primary carcinoma of the stomach, intestine, uterus, pancreas, and mammary gland. The organs whose veins empty into the portal system are naturally those most apt to distribute the cells of such neoplasms to the liver.

The condition usually occurs in the form of nodes irregularly scattered throughout the liver substance. Each has its origin in a capillary cancer embolus. The cells of these emboli grow rapidly, infiltrate the tissue, bring about atrophy of the liver-cells, and form nests and masses. As the nodules become large, umbilication of those which are superficially situated takes place from degeneration and loss of substance in the interior.

The secondary, like the primary, nodes often appear sharply circumscribed.

The type of cell found in the secondary carcinoma varies somewhat according to the parent tumor, and an examination of the cells of the secondary growth will sometimes reveal the seat of primary growth by the characteristics of the cells.

Adrenal growths sometimes occur in the liver. They depend for their formation upon fragments of tissue displaced during the differentiation of the organs. The growths are readily recognized by the characteristics of the cells, which have the usual cubical shape and contain fat and pigment, as in their normal position.

Cysts of the liver are formed by dilatation of the bile-ducts. Such a change is observed frequently in the adenocystoma. Dilatation of the lymphatics occasionally leads to cyst formation.

Echinococcus cysts are common in the liver, both in the unilocular and in the multiloeular form. The substance of the organ may be almost completely obliterated in the rare cases of multilocular cysts. (See Echinococcus Cysts.)

Parasites.—Of these, a common animal parasite in the lower animals, but rare parasite of man, is the *Coccidium oviforme*. This organism, being ingested in the spore stage, develops into an ameboid embryo in the stomach and intestine, and enters the bile-ducts, where it takes up its abode in the epithelial cells. Some of the parasites attaining adult growth are discharged in an encysted form, containing embryos; others transform themselves into sporocysts in the bile-ducts, and the infection of new cells takes place directly. The outcome of the activity of the parasites is a chronic catarrhal inflammation of the bile-ducts, with frequent cystic dilatations. The liver presents a peculiar appearance when examined with the naked eye, being studded with yellowish nodules of varying size. The organ is always deeply congested and dark-red, so that the nodules are all the more conspicuous. One is reminded of both tubercle and adenoma.

When microscopically examined, the appearance is much like adenoma, with cystic dilatation of the ducts and polypoid excrescences growing from their walls. The parasites ean be seen in the embryonal stage in the epithelial cells, and in the lumen of the ducts very numerous adult encysted parasites are present.

The *Amœba coli* also infects the liver, entering from the intestinal vessels in eases of dysentery. Its relation to liver abseess has already been described.

The *worms*—Distoma hepaticum and lanceolatum, etc.—are fully described in the general section upon Animal Parasites.

DISEASES OF THE GALL-BLADDER AND BILE-DUCTS.

Inflammation of the bile-ducts is known as **angiocholitis** or **cholangitis.** The inflammation may depend upon causes originating within the ducts, as the formation and retention of gall-stones, or upon micro-organisms brought to them by the circulating blood or ascending from the intestine. In rare cases it may depend upon worms entering from the intestine, etc.

The inflammation may be catarrhal or purulent, the former being characterized by mucus, the latter by purulent exudation. The severity of the inflammation may result in suppuration or even in gangrene, depending upon its severity. Mild inflammatory processes may occur without important changes; but severe purulent or ulcerative inflammations may cause perforation of the ducts and abscesses in the surrounding tissues, or in healing may so contract the lumen of the ducts as to cause subsequent dilatation, bile stasis, calculus formation, and predispose to further pathologic changes.

The swelling of the mucous membrane, the accumulation of inspissated secretion, the impaction of gall-stones, foreign bodies, etc., the contraction of cicatrizing lesions, the pressure exerted upon the exterior of the ducts by morbid growths, etc., all lead to retention of bile, icterus, and dilatation of the ducts, and predispose to the formation of calculi and cysts.

The cysts formed in consequence of biliary retention may be numerous, and may vary in size from a pin-head to a man's fist. The walls are smooth and very delicate, corresponding to the original epithelial lining of the bile-ducts. They may be deep in the substance of the liver or may project from the surface. The contents may consist of inspissated or scarcely altered bile, or, in old cases, of clear, colorless fluid.

Coccidiosis is a common parasitic affection of the bile-ducts of the rodents.

Cholecystitis, or inflammation of the gall-bladder, may be *traumatic*, depending upon calculi, etc., formed within it; or *infectious*, depending upon bacteria and other parasites which enter from the intestine. The most frequent cause is the presence of gall-stones. Infectious cholecystitis may be purulent.

When the cystic duct is obstructed so that bile ceases to enter the gall-bladder from the liver, the continued secretion of the glands in the walls of the bladder cause it to distend. The bile which it contains is slowly absorbed, and when the duct has long been obstructed, the bladder contains clear fluid. The distention of the closed bladder with clear fluid is spoken of as *hydrops vesicæ felleæ*. Distention of the gall-bladder with bile occurs when the common ducts are obstructed and the bile, unable to escape into the intestine, is forced into the gall-bladder.

The inflammations of the gall-bladder are in general identical with those of the bile-ducts and depend upon identical causes.

Tumors of the gall-bladder and of the large biliary ducts are not uncommon. *Carcinoma* is the most frequent and important. It is one of those tumors which seem to be intimately associated with trauma and irritation. In nearly all cases of primary carcinoma of these parts gall-stones are present, and are not infrequently impacted at the seat of disease. This makes it appear very much as if the gall-stones might be responsible for the development of the neoplasm. On the other hand, however, it must not be forgotten that in cases of neoplasm there is nearly always sufficient obstruction and biliary stasis to predispose to calculus formation.

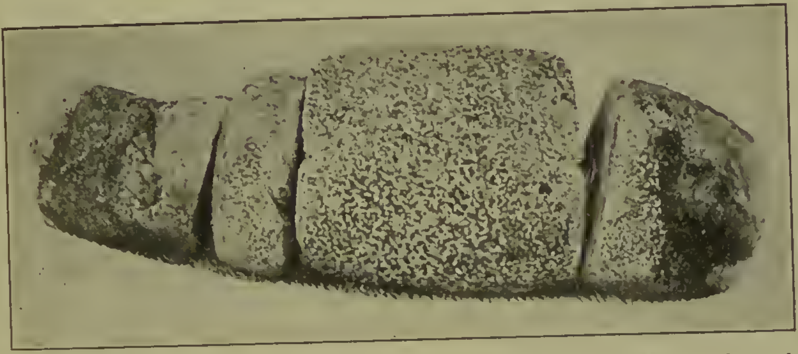

FIG. 261.—Mass of gall-stones (natural size) removed from the gall-bladder of an old woman. In this case there was no history of hepatic disorder.

The cancer of the biliary passages is a cylindric epithelioma which usually forms an irregular mass, but may form a fungous or papillary growth. The central part of the tumor frequently corresponds to some large duct and is ulcerated and eroded where a calculus impinges upon it.

Other tumors of the bile-ducts are rare. *Fibroma*, *myxoma*, and *sarcoma* have been observed.

Gall-stones or **biliary calculi** (*cholelithiasis*) are concretions formed by the precipitation of solid substances from the bile. The conditions predisposing to their formation are not entirely understood. They are very common after middle life, increasing in frequency with increase of years, and are at least three times as common in women as in men. Usually they are associated with the full-body habit suggestive of hypernutrition, though they occur in all social conditions of life. Sometimes they seem to depend upon a hereditary predisposition, certain families being particularly liable to them. Errors in personal hygiene, such as excessive eating, highly nutritious food, tight clothing, constipation, sedentary occupations; nervous diseases,—neurasthenia,—inflammations about the gall-bladder, obstructions of the duct, and malignant disease all seem to have a certain amount of influence in their production.

Gall-stones usually form in the gall-bladder, from which they may or may not enter the ducts. Stones in the ducts are usually formed in the gall-bladder, but in some cases may originate in the ducts themselves. Calculi are very rarely formed in the hepatic duct, though they may sometimes be accidentally driven into it.

There may be one stone or, as is more frequently the case, several. Sometimes the gall-bladder is full of small stones. Morgagni has seen 3000; Naunyn, 5000; and Otto has seen a case in which 7802 stones were present in one gall-bladder. Instead of well-formed calculi, the gall-bladder may contain an earthy precipitate from the bile which incrusts its walls. In some cases this mineral coating is described as "mortar-like." The size of the stones varies greatly, the largest single stone on record found by Meckel measuring 6 by 2.5 inches. A large stone found by Ritter weighed 135 grams.

The shape of the stones depends entirely upon their number: single stones are round or ovoid; multiple stones are of a great variety of shapes, being flattened by mutual contact. When a single stone is faceted, it indicates that its fellows have escaped through the ducts.

The stones usually form about nuclei, which may be flakes of mucus, masses of epithelial cells, and fibrin in inflammatory conditions, groups of bacteria, fragments of parasites, foreign bodies, etc. Upon these the component salts are deposited layer upon layer. When the substance of the stone is all of the same chemic composition, it is said to be *homogeneous;* when, as not infrequently happens, of different substances, according as one or another constituent of the bile predominates at different times during its formation, *heterogeneous* or *mixed.* When several stones are present in the gall-bladder at the same time, they usually, though not necessarily, have the same chemic composition.

The color of the stones varies with their composition, some being whitish or grayish, others greenish or brownish. A few are black; some rare stones are amber-colored.

The chemic composition of the stones varies as follows:

1. **The Common Gall-stone or Cholesterin Bilirubinate of Calcium Stone.**—It is the common gall-stone, and is usually about the size of a pea, though it may be as large as a cherry. In color it is yellowish, brownish, or greenish, or may even be brown-black. The surface is almost invariably smooth, the structure laminated, the lamina being of different colors. This varied color of the lamina is best seen at the edges of the facets. The stones are moderately soft, sometimes quite plastic. They crack and often crumble to pieces in drying. They may be single or multiple.

According to Ritter, such stones contain about 70.6 per cent. of cholesterin, 22.9 per cent. of organic matter, and 6.5 per cent. of inorganic constituents. When carefully studied, it is found that the structure is very complex, and may include cholesterin, bilirubin, bilifuscin, biliphrasin, bilihumin, carbonate of lime, phosphate of lime, ammoniomagnesian phosphate, mucus, bile acids, fatty acids, calcium manganate, calcium sulphate, magnesium carbonate, sodium chlorid, and traces of iron, copper, manganese, and uric acid.

2. **Cholesterin calculi** are rather less common.

(*a*) *Laminated Cholesterin Calculi.*—These may be yellow, brown, green, or even black in color. They usually appear translucent when fresh and moist. They may be single or multiple and are usually friable. The surfaces are smooth, often faceted. When broken, the structure is found to be laminated, but also radiated. A central nucleus may be present; when mixed with considerable calcium carbonate, they may be chalky.

(*b*) *Pure cholesterin calculi* contain about 95 per cent. of cholesterin. They are rare and usually solitary. The average size is about that of a pigeon's egg. When fresh and moist, they appear translucent, and of a pale-yellow, creamy, or amber color. The surface is usually rough, sometimes simply gritty, sometimes nodulated, like a blackberry; it may be smooth. The fractured surface is homogeneous, like a piece of gum-camphor, and shows neither laminations nor radiations. There may be a nucleus. The specific gravity is light; the substance is inflammable.

3. **Bilirubin Calculi.**—(*a*) *Bilirubinate of calcium* with added substances frequently forms calculi which may attain the size of a marble, though usually smaller. They may be solitary or multiple, are commonly faceted, and present a characteristic rusty color. Sometimes they are black. Their structure is laminated, and when they dry, they crack and often shed the outer layer, which usually contains about 25 per cent. of cholesterin.

(*b*) *Pure bile-pigment calculi* are rare in occurrence and never larger than a pea. Their color varies from rust-color to blackish. Some of these stones are rough, some nodular upon the surface. They are very friable, and when dried, may crumble. When fresh, they may be plastic.

4. **Calcium carbonate calculi** are very rare. The composition is chiefly calcium carbonate, and the color, in consequence, nearly white and chalky, especially upon the broken surface. These calculi are apt to be large in size, and are frequently associated with carcinoma of the bile-ducts.

The formation of biliary calculi is not complicated. Upon some nucleus the bile-salts and pigments are precipitated layer upon layer until the framework of the calculus is formed. The addition of the cholesterin takes place later by a process of slow infiltration, the substance crystallizing in the interstices of the stone as the organic products dissolve out. The cholesterin may also replace the bile-pigment compounds when they yield to subsequent solution. The origin of the cholesterin is a much-disputed matter, for while it forms so large a part of most of the calculi, it is present in the bile, as found by Hammarsten, in the very small proportion of 0.063 to 0.096 per cent. That the cholesterin of the larger calculi formed in the gall-bladder is precipitated from the bile seems to be impossible, so that it is now supposed, as suggested by Naunyn, that it is derived from the epithelial cells of the lining membrane of the gall-bladder. This is the only explanation for the development of cholesterin calculi in gall-bladders which are shut off from their communication with the ducts by diseased conditions (Murphy).

The natural tendency of the stones is to assume a spheric form, but when numerous, crevices are left in which layer after layer of the component salts are deposited until the stones assume the well-known faceted form. If the process continues long enough and undisturbed, the several stones may unite and form a single one. The facets upon the stones are not an indication of friction, though, of course, if the stones be disturbed by pressure upon the gall-bladder, they will glide upon one another at the approximated surfaces.

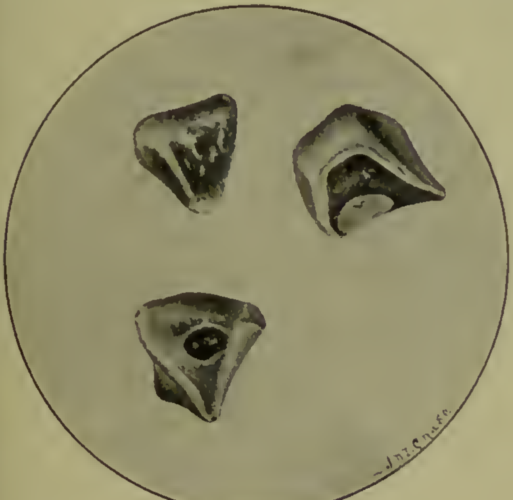

FIG. 262.—Common gall-stones.

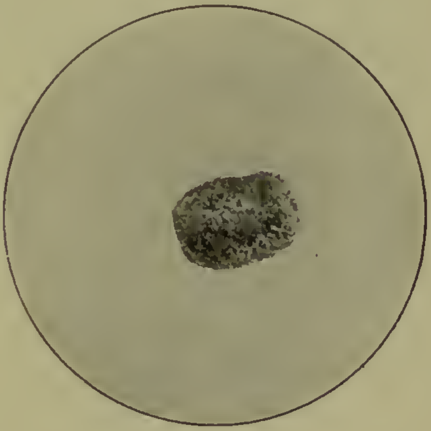

FIG. 263.—Pure cholesterin gall-stone.

The pathology of gall-stones is very important, and they may become sources of very considerable danger. The most frequent change observed is catarrhal inflammation of the gall-bladder, which may have preceded and led to the formation of the calculus, or result from its presence. The change may be slight, or it may result in the formation of a considerable mucopurulent exudate, with calcareous deposition, by which the gall-bladder becomes filled with a conglomerate mass of gall-stones, bile-pigment, cholesterin crystals, granules of carbonate of lime, and thickened mucobile. The walls of the gall-bladder may be smooth, or thickened, ulcerated, irregularly pouched, or diverticulated. The muscular walls may be degenerated or its tissues calcified. Atrophy with contraction of the gall-bladder sometimes follows these changes, and the frequent association of carcinoma and gall-stones makes pretty certain the probability that the tumor has something to do with the irritation of the calculus.

One of the most distressing clinical phenomena associated with gall-stones is that caused by their accidental lodgment in the ducts. It can never be foretold when a stone will pass out of the gall-bladder into the duct, or what particular force impells it to do so. The accident seems to occur only in connection with small stones, it being, according to Schuppel, impossible for a stone of more than 1 cm. diameter to pass into the duct. Large stones may occasionally simulate impaction by temporarily wedging themselves in the narrow part of the gall-bladder or mouth of the duct. The stones may pass through without trouble, or may be detained for a time, during which the patient suffers from muscular spasm and pain, then pass on, or they may be held permanently. The stones escaping from the gall-bladder usually lodge in the beginning of the cystic duct. In disease of the common duct stones may pass from the cystic into the hepatic duct. The ductus choledochus is usually large enough to permit the passage of any calculus that can enter it from either of the other ducts, and is, therefore, seldom the seat of obstruction. Courvoisier has collected 177 cases of obstruction of the common duct in which the calculus was situated at the beginning of the duct in 17, at its center in 19, close to the duodenum in 20, and in the papilla in 41. In 26 of the cases the duct was full of stones.

The effect of the accident is obstruction, the stone acting as a plug beyond which no bile can pass. If the stone lodges in the cystic duct, jaundice usually does not occur, and the entrance and exit of fluids from the gall-bladder are alone prevented. As the secretions of the gall-bladder walls continue, it might be supposed that, exit being prevented, the organ would dilate considerably. This is, however, not usually the case, as in 87 cases studied by Courvoisier in only 17 was the gall-bladder dilated. The probable explanation is that the repeated inflammatory reactions brought about cause a thickening of the walls of the gall-bladder by which its distention is prevented.

When the stones enter the hepatic duct, the outflow of bile from the liver is prevented and jaundice follows. There is usually much pain. If the stone is unable to move, the result of its presence is the formation of a pouch or diverticulum in the duct, the bile subsequently flowing by the partly encapsulated stone.

Stone in the common duct causes enormous distention, Frerichs having seen a case in which it was eight inches long and five inches in diameter. The dilatation not only affects the common duct, but also the hepatic duct and its radicles. It is always associated with jaundice. There are much pain and vomiting.

A very serious result of the presence of a gall-stone is ulceration through the wall of the gall-bladder or ducts. Such perforation is not at all uncommon, Courvoisier observing it in 499 out of 1800 cases of cholelithiasis.

The most frequent perforation is by ulceration through the external anterior surface of the body; the next most frequent course of the calculus is into the duodenum; next into the peritoneal cavity.

The following is Courvoisier's table of 499 cases:

Fistulous communications between different parts of the biliary system	8
Perforation of the portal vein	5
Perforation into the peritoneal cavity	70
Perforation into the peritoneal pouches	49
Perforation of retroperitoneal tissues	3
Perforation of the stomach	13
Perforation of duodenum	83
Perforation of jejunum	1
Perforation of ileum	1
Perforation of colon	39
Perforation of urinary tract	7
Perforation of pleura and lung	24
Perforation externally	196
	499

Doubtless many internal perforations are never discovered. The effect of perforation necessarily varies with the course taken by the stone. The peritoneal perforations are apt to be followed by fatal peritonitis in cases with cholecystitis of an infectious nature. Erosion of the portal vein may cause fatal hemorrhage, though thrombosis nearly always occurs. On the other hand, ulceration into the intestine may be followed by the escape of the stone by the rectum and repair of the fistula. Some of the large stones which have entered the intestine in this manner have been known to cause its obstruction. Thoracic perforations usually result in abscesses of the mediastinum. Perforation into the stomach causes vomiting and the expulsion of the calculus. The fistula may subsequently close perfectly.

One of the interesting symptoms of cholelithiasis is *fever*, which closely resembles malarial fever and is frequently called, after its observer, "*Charcot's intermittent*," or "*hepatic intermittent*." The condition begins with a chill and a rise of temperature to 104°, 105°, or even 106° F.; the patient then sweats profusely, the temperature declines, and an intermission occurs, followed by a repetition of the phenomenon. The fever seems to depend upon some leukomain retained by the calculus; as soon as the stone escapes, the fever disappears.

DISEASES OF THE PANCREAS.

Congenital malformations of the pancreas are unimportant. The organ is rarely absent, except in cases of acardia, etc.

The organ not infrequently consists of separated segments. The most frequent of these is found lying in the curve of the duodenum, and represents a separation of the head from the organ. It is sometimes called *pancreas minus*, and may have its duct (duct of Santorini) communicating with the intestine directly or emptying into the main pancreatic duct (duct of

Wirsung). Accessory pancreati are not infrequent, the most interesting consisting of small detached fragments which are situated between the coats of the stomach or the intestine, communicating with the interior of either organ by ducts of their own. These little bodies sometimes form small, tumor-like projections upon the mucous surface of the stomach or intestine, and may readily be mistaken for neoplasms. When examined microscopically, they suggest adenoma, but upon careful examination are found to have a structure identical with the pancreas.

Anemia of the pancreas is a rare pathologic condition and leads to atrophic changes.

Hyperemia of the pancreas is unimportant. It may be the preliminary of inflammation, or may result from excessive physiologic activity. Passive hyperemia may lead to some increase of connective tissue in the organ. It is frequent in alcoholics.

Hemorrhage or apoplexy of the pancreas, also called *acute hemorrhagic pancreatitis*, is a rare and peculiar affection of vague origin. It occurs into the interalveolar and peripancreatic tissues. The condition may be fatal from reflex paralysis of the heart through the semilunar plexus and nerves in the vicinity of the celiac artery. The entire pancreas is usually affected.

As causes of the affection, venous stasis, diseased vessels, tissue necrosis, inflammation, traumatism, and neoplasms may be mentioned.

In cases that recover the blood is absorbed and more or less induration follows. Cysts are occasionally formed after hemorrhage.

Atrophy of the pancreas is not infrequent and is of regular occurrence in old age. It also follows local disturbances of the circulation, marasmus, diabetes, cachexia, etc. The organ becomes reduced in size, flaccid, and is often dark in color.

The atrophic pancreas of diabetes is said by Hansemann to differ from simple atrophy in that it consists of an interstitial inflammation associated with granular kidney, etc. It leads to disappearance of the parenchyma, with increase of the connective tissue. The organ often becomes intimately united with the connective tissue of surrounding parts. Opie has found that in the pancreas of diabetes the chief change is a hyaline degeneration of the islands of Langerhans. In simple cachectic atrophy the organ is always sharply separated from the surrounding tissues. In the diabetic atrophy there is a distinct loss of thickness; in simple atrophy there is general diminution in size. The organ may be reduced to half its bulk.

Inflammation of the Pancreas.—It is doubtful whether or not there is a true parenchymatous inflammation. If so, it is seen in the cloudy swelling occurring in infectious and toxic conditions. This, however, may be only the early stage of rapid degeneration.

Acute purulent pancreatitis is a rare affection, similar to acute purulent parotitis. The organ becomes swollen, hyperemic, and of woody hardness. The purulent change may consist of a diffuse infiltration or an even distribution of miliary foci with occasional distinct abscesses. In very severe cases the entire organ may be transformed into an abscess surrounded by thickened connective tissue.

The inflammation is rarely primary, usually depending upon inflammation of contiguous organs, the most frequent being perforation of gastric ulcer and suppurative lymphangitis. Secondary necrosis and gangrene of the pancreas sometimes result in perforation of the posterior wall of the stomach.

Primary inflammation of the pancreas probably depends upon the entrance of the colon bacillus, streptococcus, or typhoid bacillus into its ducts.

Chronic pancreatitis is usually an indurating process by which the organ becomes either increased or diminished in size, very hard and dense, and often of cartilaginous consistence. The microscope shows, in addition to the increase of connective tissue, more or less atrophy of the parenchyma.

It is frequently secondary to inflammation or ulcer of the stomach, with adhesion to the pancreas.

Alcoholics often have cirrhotic pancreati. Congenital syphilitics are also said to have indurated pancreati.

Syphilitic pancreatitis and **tuberculous pancreatitis** are rare affections. In the former may be mentioned the congenital syphilitic cirrhosis of the pancreas. Gumma of the pancreas is very rare, only a few cases having been reported. Tuberculous disease occurred secondarily in the pancreas in 9 per cent. of the cases carefully studied by Kudrewetzky. The form usually seen is the miliary tubercle. Rarely large caseous excavations are seen discharging through the ducts.

Degenerations and Infiltrations of the Pancreas.—**Fatty infiltration,** or **lipomatosis,** is a rather frequent affection of the pancreas. It consists of a deposition of fat in the interlobular connective tissue of the organ, and a consequent pressure atrophy of the parenchyma of the organ. The condition occurs in obesity, and occasionally in marasmus. It may lead to complete disappearance of the pancreatic tissue. In some cases the pancreatic cells themselves show signs of fatty infiltration.

Fatty metamorphosis of the pancreas occurs in the course of severe infection and intoxication. To the naked eye, the pancreatic tissue has a cloudy white color.

Fat necrosis or **adipose tissue necrosis** is a peculiar condition sometimes seen as a result of pancreatic disease. It was first described by Balser, and is characterized by the occurrence of small, punctiform, miliary, or larger areas in the pancreas. These have an opaque grayish or yellowish color. Sometimes neighboring areas become confluent and embrace a considerable part of the pancreatic tissue. The entire organ may be involved. In the invaded areas there is first a necrosis of the fatty tissue of the pancreas, and subsequent necrosis of the adjacent pancreatic parenchyma.

When examined microscopically, the cells of the affected part are anuclear, and the fatty tissue which has undergone destruction shows fat crystals and calcareous deposits. The whole mass has a marked affinity for hematoxylin stain.

Reactive inflammation is nearly always seen about the areas; hemorrhages sometimes occur within.

Sometimes distinctly encapsulated nodes are observed, which, when opened, are filled with mushy masses of fat-crystals, calcareous matter, etc.

The necrotic tissue is not only observed in the pancreas, but also in the fatty tissue of the omentum, in the subperitoneal fat, and in the mesentery.

The experiments of Williams upon fat necrosis indicate that it depends upon the action of escaped pancreatic juice upon the fatty tissue.

Amyloid disease of the pancreas rarely becomes sufficiently important to attract attention.

Pigmentation of the pancreas occurs in alcoholics, together with pigmentation of the muscular coat of the intestine. Local pigmentations occur in consequence of atrophy and hemorrhage. The pigment is present in the epithelial cells in the form of granules of a brownish or yellowish color. The pigment seems not to contain iron. In marked cases the connective tissue may also contain pigment-granules.

Tumors of the Pancreas.—**Sarcoma of the pancreas** is rare. The few cases recorded have been of the round-cell variety. *Angiosarcoma* has also been observed. *Secondary sarcoma* is seen in cases of sarcomatosis.

Adenoma of the pancreas is frequent. The tumors usually originate as more or less circumscribed nodes, most frequently in the head, sometimes in the body, sometimes in the tail of the organ. They soon spread, and not infrequently result in the formation of a mass involving the pancreas, bile-ducts, duodenum, pylorus, and other neighboring viscera. The entire normal structure of the organ may be destroyed.

The tumors are usually firm, grayish-white in color, and are scirrhous, soft tumors being rare. Colloid cancer has been described.

The growth of the tumor about the bile-ducts not infrequently leads to obstruction and icterus. There are nearly always secondary nodes in the neighboring lymphatic glands and in the liver. The vertebral column may be eroded or infiltrated. The vena cava, vena porta, or vena mesenterica superiora may become invaded with thrombi and seriously embarrass the abdominal circulation.

The microscopic study of the tumors usually shows that the cells originate from the parenchyma of the organ. Occasionally they grow from the cylindric epithelium of the ducts.

Obstruction of the ducts of the pancreas may lead to cyst formation.

Secondary carcinoma of the organ is frequent in general carcinomatoses and from local carcinoma in the neighborhood.

Pancreatic Calculi.—Calculi are occasionally found in the pancreatic ducts in the form of coarse grains distributed throughout the system of ducts, or as distinct oval, smooth, or nodulated concretions. They may be single or multiple. The chief ingredients, like those of the salivary calculi, are carbonate and phosphate of lime. The shape of the calculi is sometimes very peculiar, as they usually form incrustations upon the ducts and often have patulous centers, and may appear branched, corresponding to the ducts in which they are formed. They usually excite more or less inflammation of the affected parts, sometimes suppurative, sometimes cirrhotic. Not infrequently the result of their presence is obstruction of the duct, with retention of its secretion and the formation of pancreatic cysts or *pancreatic ranula*.

Obstruction of Wirsung's duct can occur in consequence of morbid growths, calculi, cicatrices, and inspissated secretions. The usual result of the obstruction is dilatation and cyst formation. The cysts more commonly involve the branches than the main duct, and are more frequent in the head of the pancreas than elsewhere. They contain clear fluid or the contents may be inspissated. Rarely they are purulent.

DISEASES OF THE PERITONEUM.

Occasional **congenital malformations** of the peritoneum are seen. Sometimes the funicular portion of the peritoneum fails to unite, after descent of the testicle into the scrotum, leaving a permanent communication between the peritoneal cavity and cavity of the tunica vaginalis testis. At times the omentum is absent or very small; at other times it is unusually large and relaxed, so as easily to descend into a patulous inguinal canal. The mesentery not infrequently shows variations in its length.

In cases in which the peritoneum is not normally developed the movement of the intestines may be interfered with. Openings in the mesentery or omentum sometimes occur, and may be occasional causes of strangulation in internal hernias.

Hyperemia of the peritoneum precedes the early stages of inflammation.

Passive hyperemia is of little importance. It is seen in cirrhosis of the liver and in other affections with portal congestion. Dilatation and tortuosity of the veins are observed, together with small hemorrhages into the subperitoneal tissue.

Hypostatic congestion can be seen at autopsy upon the serous surface of links of the intestine which occupy the dependent parts of the cadaver.

Hemorrhage into the subperitoneal tissue is common in the form of petechiæ and irregular blotches and stripes, especially along the vessels of the mesentery and omentum. They occur in asphyxia, in passive congestion, and in certain intoxications and infections.

Hemorrhage into the peritoneal cavity follows rupture of the blood vessels. It is seen in many traumatic injuries with rupture of the viscera, follows rupture of abdominal aneurysms and extra-uterine pregnancy with rupture of the cyst, and rupture of the spleen in leukemia and malaria.

The blood descends to the dependent parts of the peritoneal cavity, and if the patient lives, undergoes absorption. Even when the blood coagulates, it causes no particular irritation and is readily absorbed, causing no permanent changes. Adhesions may succeed peritoneal hemorrhage with coagulation.

Should bacteria enter simultaneously with the escape of blood into the peritoneum, the results are less favorable, peritonitis being the certain outcome.

Ascites or serous fluid in the peritoneum is a very common affection. It occurs in hydremic conditions in kidney disease, in various cachectic diseases, in pulmonary and cardiac diseases, but, above all, in obstruction of the portal circulation. The most frequent is cirrhosis of the liver. It may also occur in such local diseases of the peritoneum as tuberculosis, sarcomatosis, etc.

The dropsical condition is, in most instances, the result of increased transudation from the blood vessels. In cases of tuberculosis and sarcomatosis it may have something to do with obstructive changes in the lymphatic circulation.

The quantity of fluid contained in the peritoneal cavity may reach several gallons. It is a clear, straw-colored fluid, much like normal urine in appearance. In rare cases it is colorless. It very rarely appears like milk, from admixture with chyle. The fluid contains albumin—less than 3 per cent. It does not coagulate spontaneously.

In cases of **hydrops of the peritoneum** the membrane itself may be normal in appearance, but is usually changed by maceration and infiltration so as to be dulled upon the surface and somewhat thickened. The subperitoneal cellular tissue and fat may be edematous and translucent, like jelly. Sometimes, when of prolonged duration, it is studded with minute grayish-white dots consisting of granulation tissue. These are indistinguishable from tubercles by the unaided eye.

Sometimes the fluid accumulates beneath the peritoneum, between it and the muscular tissues. This was called *hydrops peritonæi* by the older writers, in contradistinction to *hydrops omenti*, when the fluid accumulations occurs between the layers of the omentum.

"**Milk spots**" upon the peritoneal surface of organs are very frequent. They resemble the "milk spots" or friction scleroses of the heart, but are usually more extensive and much thicker. They may calcify, and beneath a smooth or sometimes rather porous-looking surface, a free distribution of lime-salts may be present. These spots are most common upon the spleen, next most common upon the diaphragmatic surface of the liver. The mode of their formation is uncertain. It seems impossible that friction can explain it.

Acute peritonitis may be of *primary* or *secondary* origin. Birch-Hirschfeld divides them into:

PRIMARY—Idiopathic.
SECONDARY—1. Metastatic.
2. Continuity.
3. Perforation.

Primary acute peritonitis is supposed to be of hematogenous origin and to depend upon the transportation of pyogenic bacteria from remote parts of the body—felons, leg-ulcers, etc.—to the peritoneum, where an acute inflammatory process is established. It sometimes occurs in nephritis, polyarthritis rheumatica, pyemia, and rarely in the acute exanthemata. In rare cases peritonitis occurs spontaneously—*i. e.*, without any primitive lesion. It is only this form that Birch-Hirschfeld would regard as primary, the others being metastatic and secondary.

Secondary acute peritonitis is much more frequent and depends upon local damage of the peritoneum, brought about by traumatic injuries and by diseased, especially suppurative, conditions of the various organs. Bacteria, of which the Streptococcus pyogenes, Bacillus coli communis, Staphylococcus pyogenes aureus and albus, and pneumococcus are the most frequent, are exciting causes. The disease is set up by continuity of tissue and invasion through the lymphatics.

The lesions most frequently predisposing to peritonitis are puerperal infections of the female genital apparatus, perforating ulcer of the stomach and intestine, especially of the vermiform appendix, inflammation of the intestine, stomach, liver, gall-bladder, spleen, internal sexual organs, bladder, pancreas, kidneys, spinal column, pelvis, pleura, diaphragm, ulcers of the intestines descending to the serosa, gangrene of the intestine or omentum, and such internal accidents as intussusception, volvulus, strangulated hernia, etc.

Peritonitis in new-born children may depend upon septic infection of the umbilicus.

The morbid appearances will vary according to the severity, extent, and duration of the affection. It may be a purely local affection, limited to narrow confines above and about an intestinal ulcer or other small lesion; it may invade an extensive region of the abdomen, as in typhlitis and appendicitis, or it may be general to the entire peritoneum.

The inflammation begins with hyperemia, but soon is characterized by a serous or serofibrinous exudation, which becomes purulent. Many cases are purulent from the beginning. Sometimes they are serous, with a few floating fibrin flocculi; sometimes they are hemorrhagic.

When the amount of exudation is small and the severity of the case not great, the inflammatory exudation is seen to spread over the most affected parts, in the form of a whitish, creamy layer. The surface of the intestines is always dulled, from hyperemia and alteration in the endothelial cells of the serosa. A creamy layer of fibrin and leukocytes usually clings to the surfaces of the organs.

If the disease is more wide-spread and the exudation more considerable, it collects in the form of purulent liquid in the dependent parts of the abdominal cavity, or in pockets between partially adherent surfaces of intestine, omentum, abdominal wall, etc.

In severe cases the peritoneum shows distinct signs of maceration, infiltration, and partial disorganization. This is probably best seen upon the serosa, which may be transformed to a softened, discolored, easily lacerable tissue, which can often be stripped off of the subjacent muscular coat.

Adhesions are early formed between adjacent loops of intestine, between intestine and abdominal wall, between the stomach and liver, etc. These originally consist only of sticky fibrin, but are transformed to connective tissue during the process of repair.

In the purulent peritonitis which usually follows perforation of the intestine the pus separates into liquor puris and corpuscles, the latter sedimenting in the dependent parts of the abdominal cavity. When there is subsequent escape of fecal matter into the abdominal cavity, the pus very often has an exceedingly disagreeable fetid odor, and the abdomen may contain gas, which escapes with an audible sound when the cavity is opened.

Local peritonitis usually recovers. The exudate is absorbed, as a rule, but when there has been much suppuration, an abscess usually forms. This may rupture externally or into the bowel, or may remain for a long time encapsulated.

General peritonitis is commonly a fatal affection. When recovery occurs in either local or general peritonitis, an almost constant sequel of the inflammatory process is the formation of *adhesions*, where fibrin has glued adjacent surfaces of peritoneum together. As time passes the adhesions yield to traction and finally appear as fibrous, sometimes almost tendinous, cords. They may be so numerous as to bind together most of the abdominal viscera, and the intestine may lose its free tubular form and become fixed and united into a mass that resembles a solid organ with a tortuous canal passing through it. The omentum is drawn up early in peritonitis, leaving the surface of the intestines exposed. It later suffers union of its component layers and adhesion to neighboring organs.

The capsules of the abdominal organs are sometimes thickened by the peritonitis; more frequently, however, in chronic than in acute peritonitis. When the union between contiguous surfaces of the inflamed peritoneum takes place early, it may save the patient from the spread of disease by localizing it, an abscess forming between the layers.

In rare cases of recovery from general purulent peritonitis the pus from the abdominal cavity may be externally discharged by rupture at the umbilicus, especially in children.

In cases of resorption collections of pus may remain for a long time here and there, and eventually be discharged by perforation into the intestine. Such collections may remain encapsulated.

Chronic peritonitis may result from the acute form by failure of the exudate to undergo complete absorption, so that collections of encapsulated pus remain to continue the irritation and form unions with the surrounding organs and tissues or cover them with thick fibroconnective-tissue membranes.

Chronic local peritonitis also occurs in consequence of chronic disease of the organs, and leads to fibrous thickenings of their capsules. This is particularly the case with the liver—perihepatitis—and the spleen—perisplenitis.

The disease seems to be especially common in the neighborhood of the female genital organs, where the uterus, ovaries, and tubes become united with each other and are dislocated, thickened, and distorted by its course.

At times it may be general and extend over the entire peritoneum, developing without any apparent cause and leading to the formation of adhesions and thickenings everywhere.

Chronic peritonitis always accompanies tuberculosis, and is frequent in some of the neoplasms of the peritoneum. In the chronic peritonitis which so frequently occurs in neoplasms of the abdominal viscera a peculiar thickening of the capsules of the spleen, liver, and other organs, which become thick, white, and smooth, the sharp edges being rounded off, is often seen. This is suggestive of the icing upon a cake, and has, in consequence, been called by the Germans "Zuckerausguss," or icing.

Tuberculosis of the Peritoneum.—This is a frequent affection, which occurs in about 15 per cent. of cases of well-marked tuberculosis.

Hematogenous tuberculous peritonitis is not infrequent in tuberculosis of the lungs and other organs. The tubercle bacilli are distributed through the blood, and lead to the formation of miliary tubercles.

To the naked eye the tubercles appear as small, circumscribed, grayish or yellowish dots studded over the peritoneal surface. They may occasion little general inflammation, and the disease may progress unobserved and unsuspected, but in most cases there is a dropsical effusion. Uncomplicated cases are unaccompanied by suppuration, and when the abdomen contains pus, the additional presence of the streptococci and staphylococci may be expected. These cases are called *exudative tuberculous peritonitis*.

Lymphogenic tubercles are of frequent occurrence in consequence of local tuberculosis. Thus, in nearly all cases of tuberculous enteritis with ulcerations, one finds miliary tubercles along the lymphatic vessels, extending around the intestine in an annular manner or radiating in all directions. Very often the vessels themselves can be observed as grayish lines, with gray or yellow miliary tubercles here and there. The tissue surrounding the tuberculous invasion may be hyperemic and may contain occasional small hemorrhages. Fibrin may be deposited upon the serous surfaces so affected. The usual grayish or yellowish color is occasionally replaced by a slate-colored discoloration.

Adhesions are frequent in tuberculosis of the peritoneum, especially in the cases with considerable exudation, and result from coëxisting simple peritonitis, rather than from the tuberculous process itself. Tubercles, however, frequently form in the adhesions. In well-marked cases the loops of intestine may be bound together and smoothed over into a solid organ; the omentum rolled up and everywhere adherent; and the liver, spleen, and stomach covered with miliary tubercles and adherent to each other and to the diaphragm.

The female sexual organs are particularly prone to suffer from agglutinative changes when affected with local peritonitis, and in tuberculosis they are frequently so densely massed and tightly adherent as to be almost unrecognizable.

Tuberculous peritonitis may recover, though the conditions governing its recovery are unknown. Curiously enough, it seems that surgical manipulation of the abdominal cavity in some way favors convalescence. The tubercles recover by granulation and cicatrization; the exudation is absorbed, but the adhesions, of course, remain.

In tuberculous peritonitis the mesenteric and retroperitoneal glands are commonly affected. They are nearly always enlarged and studded with gray or yellow, cheesy tubercles.

Tumors of the Peritoneum.—*Primary tumors* are less frequent than those of metastatic origin or due to direct extension by continuity of tissue.

Of the connective-tissue tumors, *fibroma*, *lipoma*, *myxoma*, *sarcoma*, *angiosarcoma*, *lymphangioma*, and *chylangioma* have been observed.

The **lipoma** usually develops from an epiploic appendix and forms a pedunculated tumor, prone to calcareous infiltration, and is sometimes set free in the abdominal cavity by rupture of its pedicle.

Multiple angiomata have been seen by Rokitansky.

Endothelioma is one of the most important tumors of the peritoneum. It is of not infrequent occurrence. It is with difficulty in most cases that the primary seat of this tumor is recognized, but it is probably frequent in the omentum. It is rarely a localized tumor, but readily distributes over the peritoneum, so that when the body is examined after death, the retracted omentum is occupied by a tumor-mass as large as a man's hand, which forms the chief neoplastic development. Here and there in the mesentery, broad ligaments, gastrosplenic, gastrocolic, and other omenti similar but smaller and often multiple nodes are observed, some discrete, but the greater number connected by intermediate bands or bridges of tumor growth. The entire visceral and rarely the parietal surface of the peritoneum is more or less thickly studded with miliary or pea-sized nodules, and the surfaces of the larger organs, such as the liver, may be covered with a thick neoplastic layer like an icing ("Zuckergussleber").

Carcinoma of the peritoneum is always secondary to carcinoma of the abdominal viscera. The tumor is characterized by a wide-spread distribution of nodules of all sizes, many of them miliary in appearance, studding the surface of the intestine and mesentery, others larger and flatter, occurring upon the surfaces of the organs, large masses occupying the omentum. Confluent growths upon the liver and spleen cover them with the characteristic "icing." The peritoneum between the nodules may not be altered or may be thickened and hyperplastic. There may be distinct peritonitis, and adhesions are not infrequent. This universal peritoneal distribution of carcinoma is spoken of as "*carcinomatosis*."

The appearance of colloid carcinoma of the peritoneum is very pretty, for the degenerating cells of the nodules produce colloid masses which appear like clear drops of yellowish or colorless transparent jelly. The cavity of the peritoneum may contain much free colloid jelly escaped from the honeycombed degenerated tissue.

Cylindroma of the peritoneum occurs at times, and was described by Waldeyer as "*plexiform angioma*" of the peritoneum.

Secondary sarcoma is much less frequent than secondary carcinoma in the peritoneum. In some cases multiple minute nodules, "*sarcomatosis*," are observed, but the cases are rare.

Cysts of the peritoneum are sometimes formed by the colloid or mucoid degeneration of tumors. Most of the cysts with epithelial lining occur in connection with the ovaries and tubes.

Enterocystoma is a congenital cyst formed by imperfect development of the intestine.

Cysts lined with endothelium are sometimes very numerous, so that the abdominal cavity contains many pedunculated, grape-like, pea-sized, grape-sized, or larger bladders. These usually result from the dilatation of lymphatic vessels—*chylous cysts* or *cystic lymphangiomata*.

Of the parasitic cysts, the *echinococcus* sometimes occurs. Parasitic cysts containing worms are common in the peritoneum of rodents. Dermoid cysts in the abdomen are very frequent, but usually grow from the ovaries. A few dermoids of the omentum are on record.

CHAPTER IV.

DISEASES OF THE RESPIRATORY SYSTEM.

DISEASES OF THE NOSE.

Rhinitis.—Acute catarrhal rhinitis, or acute inflammation of the Schneiderian membrane, is one of the most common affections, especially in the acute form known as "cold in the head," or *coryza*.

Etiology.—Coryza is usually attributed to "cold." It may be a specific infectious disease, but the attempts of various observers to find specific bacteria in the secretions have failed. Many bacteria are always present, and among them some of the familiar bacteria of suppuration, but none occurs so regularly or in such numbers as to suggest specificity. As coryza is ushered in by constitutional as well as local symptoms, it is well to be cautious about regarding it as a local affection depending upon micro-organisms. It may possibly depend upon the absorption of poisonous products from the intestine or other non-infectious agencies. Acute catarrhal rhinitis is sometimes set up by the inhalation of irritating substances, such as pollen, soap-bark, ammonia, etc., and is one of the first symptoms of measles, epidemic influenza, etc. Acute catarrhal rhinitis of a severe type also sometimes results from traumatism and from the inhalation of irritating substances, or may be micro-organismal in cases of infection by the gonococcus and in the purulent forms of scarlatina, small-pox, and other diseases.

The anatomic lesions accompanying the affection are few and by no means well characterized. The mucous membrane is congested, and the glands in process of active secretion. From the nose there is a profuse serous, mucoserous, or mucopurulent discharge. When this discharge is examined microscopically, some desquamated epithelial cells and leukocytes are found.

Chronic catarrhal rhinitis usually follows frequently repeated attacks of the acute form, but not infrequently occurs in consequence of congenital or acquired deformities of the nose, such as deflected septa, misplaced nasal bones, or from the presence of polypi, morbid growths, foreign bodies, tumors, etc., and in some cases in consequence of scrofulous and syphilitic diatheses. The excessive use of tobacco is also said to be a not infrequent cause. Climate, the inhalation of irritating dusts and vapors, and impediments to respiration may also produce it. Two chief forms are described:

1. The *hypertrophic form* is marked by thickening, congestion, and swelling of the mucous membrane, and distention of its veins, especially over the turbinated bones. The epithelium becomes hyperplastic, without much tendency to desquamate. The glands of the mucosa enlarge and become hyperfunctional. The secretions from the nose are unusually viscid and mucopurulent. The nasal passages are obstructed by enlargement of the lower turbinated bones and swelling of the mucous membrane of the septum. There is commonly hypertrophy of the adenoid tissue of the upper part of the pharynx; the patients usually breathe through the mouth. As the condition persists there is considerable hyperplasia of the connective tissue beneath the mucosa, especially about the large veins. Myxomatous

formations resembling polypus may be observed over the anterior end of the middle turbinated bone.

2. The *atrophic form* may follow the hypertrophic form, or may occur as a primary affection. It leads to an enlargement of the nasal cavities, with the secretion of a purulent, yellowish or greenish material, which, from the presence of numerous saprophytic bacteria, has a disgusting odor (*ozena simplex*), and dries upon the walls of the cavity, forming discolored, greenish or bloody scabs and crusts. These do not interfere much with respiration, as the size of the cavities is increased. The ciliated epithelium of the mucous membrane is lost, and becomes replaced by squamous epithelium; the bones of the nose may atrophy in chronic cases. Ulcers are rarely formed, but erosions are common. The erectile tissue may be replaced by newly formed connective tissue, and the columnar epithelium replaced by squamous. Simple membranous rhinitis occasionally follows operations on the nose and the application of the actual cautery.

Diphtheritic rhinitis is generally secondary to the ordinary pharyngeal form of diphtheria, but may be primary. The disease may be true diphtheria, or may depend upon other micro-organisms, as the streptococcus, in scarlatina and erysipelas. The hyperemic mucous membrane in diphtheritic rhinitis is covered by a pseudomembrane which has a grayish or a yellowish-gray color, and forms a more or less continuous layer. There is a discharge, which may be mucopurulent or at times blood tinged. The specific micro-organism of diphtheria, when present, can be demonstrated by the ordinary bacteriologic examination.

Syphilitic rhinitis is rare, except as syphilitic coryza. The primary lesion has very rarely been seen. There are no distinctive features by which to recognize syphilitic rhinitis, the affection consisting simply of erythematous patches and papules that may ulcerate and lead to necrosis and exfoliation of the cartilage and bones. Gummatous inflammations sometimes occur beneath the periosteum or perichondrium of the nasal tissues, and bring about a deep-seated and destructive ulceration of the soft parts. The severity and, indeed, the naked-eye appearance of the condition are characteristic. Still more so are those cases in which there is a more or less circumscribed destruction of the bone and cartilages, followed by a sinking-in of the entire nose and the resulting deformity well known as "*saddle nose*." These inflammatory conditions are commonly associated with the putrefaction of the purulent secretions retained within the nose (*ozena syphilitica*). Drying of the purulent matter upon the walls of the nasal cavity causes the formation of dirty-looking crusts which are removed with some difficulty and frequently leave abrasions. The gumma seems to select the septum as its point of most frequent occurrence, and not infrequently leads to its perforation. Sanger describes a primary syphilitic caries of the nasal bones.

Tuberculous rhinitis is rare. The condition leads to the formation of submucous tubercles, which may soften and ulcerate and eventually lead to caries of the bone and cartilages, accompanied by a stinking discharge (*ozena tuberculosis*). Tubercle bacilli are present in the discharges. The tuberculous ulcers are most common in the lower part of the nose upon the cartilaginous septum. The primary tubercular lesions of the nose are not infrequently polypoid in form.

Leprous Rhinitis.—It is thought by Sticker that the primary infection in lepra usually takes place in the nose. The nasal lesions are constant in both the nodular and anesthetic form; the relapses of the disease always begin with nasal symptoms, and the lepra bacilli are first found in the nose. The diseased is characterized by the formation of erythematous patches and nodules. There are not infrequently ulcerations, and there is a mucopurulent discharge. The disease may extend into the frontal sinuses, and has been known to penetrate the skull and lead to fatal meningitis.

Glanders of the nose, which sometimes occurs in the human subject, is characterized by a purulent or sanguinopurulent catarrh. In the mucous membrane circumscribed nodules and wide-spread infiltrations occur. These suppurate and lead to the formation of multiple ulcerations, which may unite, extend to the deeper tissue, expose the bone, and lead to a fatal termination.

Tumors of the Nose.—The majority of these are known to clinicians and surgeons as *polypi*. Four kinds are usually described: the mucous, the adenomatous, the cystic, and the telangiectatic. All consist of a stroma of myxofibrous tissue, in which are numerous mucous glands and upon which is reflected the Schneiderian membrane.

The different polypi are sufficiently well described by their names. They are usually pedunculated, often multiple. They most commonly arise from the mucous membrane covering the middle turbinated bone. The myxomatous polypus is of most frequent occurrence.

Fibroma, myxoma, sarcoma, chondroma, osteoma, and **osteofibroma** are all occasionally met with in the nose. The fibroma may be highly vascular, and give origin to severe hemorrhages. Carcinoma sometimes develops from the mucous glands, but the most common malignant tumor of the nose is the *squamous epithelioma*, which develops from the skin of the upper lip and alæ nasi. Tumors of the nose not infrequently bring about a deformity of the nose well known as "*frog face*," by distending the nasal cavities.

Papilloma is rare in the nares, and forms only about 15 per cent. of the benign tumors. The **chondroma** is very rare. **Osteoma** grows from the nares and accessory sinuses, producing deformity in some cases.

Adenoma is uncommon. **Angioma** is also a rare tumor, usually with a myxomatous stroma.

Sarcoma is the most frequent malignant tumor of the nose, developing from the septum, floor, and outer wall. It grows rapidly, and is prone to bleed at the slightest touch. It is almost always a single tumor, sessile, soft, dark red, and vascular. Its presence is accompanied by a fetid discharge.

The **carcinoma** usually begins as a soft papule of reddish color. It is prone to undergo early ulceration, and then presents elevated, infiltrated edges and a sanious base. It causes an early swelling of the lymphatics.

Tumors of the antrum of not infrequent occurrence are myxoma, sarcoma, and fibroma. Cysts are occasionally seen.

Myiasis.—Flies sometimes cause great suffering and even death by depositing their eggs or larvæ in the nose. Such a parasitic invasion is rare and rarely takes place outside of the tropics. Leeches, centipedes, earwigs, and other insects have entered the nasal cavities and caused considerable suffering until removed.

Foreign Bodies.—Children not infrequently introduce foreign bodies, which, if not soon expelled, may become the cause of chronic inflammatory conditions.

Rhinoliths.—In nearly all diseases of the nose there are discharges of varied character, which not infrequently are retained within the nose and its cavities, where they inspissate and form crusts. These crusts, and also sometimes foreign bodies accidentally gaining entrance into the cavities of the nose, form nuclei upon which successive layers of secretion sometimes dry, or upon which successive layers of mineral matter are deposited from the secretions, so that concretions, of which lime is usually the most important mineral constituent, are of common occurrence in the nose. These concretions or calculi are known as *rhinoliths*.

The antrum and the frontal sinuses are subject to catarrh and acute and chronic purulent inflammations.

Some mucous accumulations known as **mucoceles** are observed.

DISEASES OF THE LARYNX.

Acute catarrhal laryngitis is a simple catarrhal inflammation of the larynx. It is more easily recognized during life by the aid of the laryngoscope than on the autopsy table after death.

Etiology.—The acute cases of laryngitis are commonly attributed to cold and exposure and the inspiration of extremely hot or cold air, irrespirable gases, and irritating dusts. Many cases are infectious and secondary to infections in the mouth, pharynx, or lung.

Morbid Anatomy.—It is characterized by redness and swelling of the mucous membrane, a primary arrest of secretion, and later by the secretion of a seromucous or sometimes purulent exudate. It is exceedingly common, and usually affects the whole larynx, though occasionally it may be localized and appear only on the epiglottis, vocal cords, etc. When the cause is of continuous operation and the conditions do not speedily return to normal, a *chronic laryngitis* develops. The vessels of the organ remain widened, the epithelium becomes desquamated, attempted regeneration causes the formation of more or less thickened patches, and submucous infiltrations with round-cells lead to the formation of circumscribed or diffused thickenings. When the tissue is examined microscopically, the only important change is a round-cell infiltration.

Granular laryngitis is accompanied by enlargement and widening of the mucous glands on the lower side of the epiglottis, false vocal cords, and in the ventricles of the larynx. It is a not uncommon affection, and leads to a granular appearance of the tissues. In cases of long duration ulcers and erosions of the superficial tissue may occur upon the vocal cords and posterior commissure, probably from a collection of bacteria upon the eroded surfaces. Occasionally, when the inflammation is traumatic and violent, *acute edema of the glottis* results from a serous infiltration of the inferior surface of the epiglottis and the aryteno-epiglottidian folds, causing swelling of the mucous membrane extending to the vocal cords, and followed by such deformity as to close the air-passages. The acute edema is quite frequently unilateral, occurring as it does from ulcerations of traumatic, inflammatory, or malignant origin. In this way it can be separated from chronic edema of the larynx which results from cardiac failure, emphysema, compression of the veins of the neck, and similar causes. This form is always bilateral and symmetric.

If the acute inflammation is the result of croup, diphtheria, gangrene, tuberculosis, or syphilis, a rapid phlegmonous infiltration of the submucous tissue of the organ may occur, with the formation of mucous and submucous abscesses. This phlegmonous inflammation may extend so deeply into the cartilaginous tissue as to produce *perichondritis*. The abscesses may rupture internally in the larynx, or externally in the pharynx, esophagus, or exterior of the neck. In rare cases *tonsillitis* and traumatism may be the cause of phlegmonous laryngitis, or such a condition may occur in the course of typhoid, scarlatina, and pyemia.

Chronic Laryngitis.—The chief characteristics which mark the transformation of the ordinary into the chronic form of laryngitis are vascular dilatation, hypertrophy of the mucous membrane in all its layers and elements, and alteration of the secretion. Sir Morell Mackenzie has applied the term *phlebectasis laryngea* to that form of chronic laryngitis chiefly characterized by venous dilatation. Türck has spoken of a *chorditis tuberosa* in which the vocal cords appear nodular. It occurs in the larynges of professional singers and criers. *Laryngitis granulosa* is a very frequent accompaniment of the granular form of pharyngitis. Its appearance differs somewhat from the pharyngeal form, because of the difference in the amount of lymphoid tissue in the organs, the pharynx being particularly rich in disseminated lymphoid tissue, while the larynx contains comparatively little or none at all on the vocal cords.

Pachydermia, diffusa laryngis is a name given by Virchow to a chronic productive inflammation of the larynx which is not uncommon in criers and singers. The condition is recognized by a bluish-white discoloration and thickening of the vocal cords, most noticeable at the posterior commissure. The bluish color depends upon a pellicle consisting almost exclusively of squamous epithelial cells, which, when grasped with the forceps, can be divulsed, leaving an entirely normal mucous membrane. In severe cases the mucous membrane itself thickens, not only upon the vocal cords, but also on the side walls of the larynx, taking on a grayish-white color, and becoming dense and hard. Sometimes, instead of the smooth appearance described, one notices that the surface of the laryngeal membrane is irregular and covered with projecting warts. This form is sometimes called *pachydermia verrucosa*. Orth regards the pachydermia verrucosa as closely analogous to tumor formation.

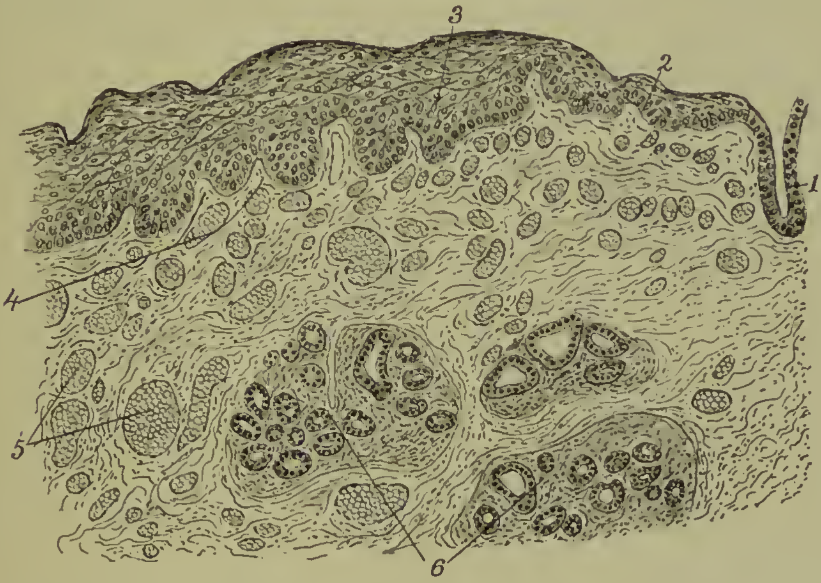

FIG. 264.—Pachydermia laryngis: 1, Cylindric epithelium; 2, area of transition into (3) stratified squamous epithelium; 4, papillary body; 5, dilated blood-vessels of tunica propria; 6, mucous glands (× 60) (Dürck).

Specific Inflammations of the Larynx.—1. **Diphtheria.**—Diphtheria may be primary in the larynx, or may follow diphtheria of the pharynx. Whether primary or secondary, the disease is characterized by the formation of a somewhat firm, whitish or yellowish-white pseudomembrane, which may occur in a single small area, in scattered patches, or as a continuous layer upon the inner surface of the larynx.

As is usual with the diphtheritic membrane, it consists of a coagulation necrotic mass, composed of fibrin and entangled epithelial cells and leukocytes. It may be loosely attached to the mucous membrane of the larynx, or may be intimately adherent to it, so that when divulsed, a red and moist surface remains. The adherence of the membrane is likely to be more intimate in those parts of the larynx which are covered by squamous epithelium. The membrane may extend from the aryteno-epiglottidian folds to the true vocal cords, or may be continued into the ventricles of the larynx and even into the trachea, and sometimes even extends down the trachea into the bronchi. Osler speaks of having seen cases in which there was no distinct membrane, but simply a friable granular deposit. The vocal cords seem particularly predisposed to the occurrence of the membrane. Next to this, perhaps, the under side of the epiglottis and the aryteno-epiglottidian folds. When recovery takes place, the membrane is apt to detach in larger or smaller pieces, according to its tenacity and the rapidity of recovery, so that at times, and especially after the use of antitoxic serum, the entire membrane may be detached in one piece, corresponding in shape to the entire cavity of the organ.

All pseudomembranous inflammations of the larynx are not necessarily true diphtheria. Experimental studies made by Reitz, Oertel, and others have shown that the inhalation of ammonium, chlorin, steam, etc., may produce pseudomembranous exudates, and the occurrence of the streptococcous pseudomembranous inflammation is now well known. The staphylococcus and colon bacillus likewise occasionally produce pseudomembranous inflammation of the larynx.

2. **Typhoid Fever.**—Typhoid fever is usually accompanied by catarrhal laryngitis, characterized by the usual signs, together with desquamation of epithelium, occasional ecchymoses, and erosions upon the borders of the epiglottis. A pseudomembranous condition sometimes occurs. Ulcerations are unusual.

Eppinger has called attention to certain diffuse or nodular soft swellings of the mucous membrane, which are formed by a submucous cellular infiltration. They usually occur at the base of the epiglottis, on the false vocal cords, and on the anterior commissure. They not infrequently ulcerate. He is of the opinion that these formations are analogous to the typhoid ulcerations of the intestines.

3. **Variola.**—Small, whitish, punctiform spots or small nodules, formed, in part, of degenerated epithelium, and, in part, of cellular infiltrations, are very common in the mucous membrane of the larynx in small-pox. Pseudomembranous inflammation sometimes occurs. Occasionally, in the later stages of the disease, little hemorrhages, minute submucous abscesses, and perichondritis may develop.

4. **Tuberculosis.**—Tuberculous laryngitis is one of the most common forms, and occurs as a primary as well as a secondary process. The secondary form of the disease, which probably most frequently results from the passage through the larynx of infectious material from the lung, is the more common of the two. The disease usually manifests itself in the form of miliary tubercles appearing as small whitish or grayish, slightly projecting subepithelial nodules. These either undergo hyperplasia of the submucous tissue with the formation of projecting nodules, warts, or actual tumors, or else soften and ulcerate. The degeneration of the tuberculous tissue occurs with greater rapidity upon the vocal cords than elsewhere.

There seems to be no rule for the course which the disease shall run: ulceration sometimes follows rapid softening, and leads to the formation of larger or smaller, slightly or deeply excavated, irregular-shaped ulcers, with infiltrated projecting, and sometimes overhanging, borders, and a base covered with a grayish or yellowish layer. There is no rule for the occurrence of these tuberculous ulcers, their distribution being purely accidental. At other times the tuberculous inflammation is distinctly productive, and smaller or larger projecting papillomatous masses are found upon the vocal cords or the walls of the larynx. In rare cases distinctly circumscribed, projecting, rounded and smooth, tumors are found, varying in size from a pea to a hazelnut. These may be either solitary or multiple. Microscopically, they consist of rather dense fibroconnective tissue containing tubercles.

The microscopic lesions may assume any of the described forms. They are commonly situated at the posterior commissure, upon the arytenoid cartilages, the aryteno-epiglottidian folds, the ventricular bands, the true cords, and rarely upon the epiglottis. The slowly spreading form of tuberculosis spoken of as *lupus* is most common upon and near the epiglottis. It extends to the neighboring structures, producing a nodular infiltration of a hyperplastic and deforming character. Ulcerations are the ultimate outcome of the process.

According to Birch-Hirschfeld, the tubercles are always to be found in the mucous and submucous layer, never descending so low as the mucous gland layer. As they increase in size, however, they go deeper and deeper, until not only the soft tissues, but also the cartilages themselves, may be affected. The larynx in tuberculous laryngitis always manifests a considerable catarrh with its associated features. In rare cases edema of the glottis and phlegmonous inflammations are found.

In *lupus of the larynx* miliary tubercles form in conglomerated groups upon a somewhat hyperemic mucous membrane, so that uneven, nodulated patches are formed. Histologically, however, this is identical with the other tuberculous lesion.

5. **Syphilis.**—Syphilitic diseases of the larynx may be very mild or very severe, and pass through all the intermediate grades. Any of the syphilitic lesions may occur in the larynx, though some are more common than others.

Primary lesions are rare, only one or two cases being on record.

Erythemata occur chiefly in the secondary stage and are most common during the fourth to the sixth month.

Mucous patches are extremely rare, and are encountered in the beginning of the secondary stage, from two to three months after infection.

Superficial ulcerations and erosions develop from the mucous patches.

Gummata are common.

Deep ulcerations follow the gumma.

Cicatrices occur in the process of healing and may be so severe as to lead to stenosis.

The most simple and most frequent form of syphilitic laryngitis is the ordinary *laryngeal catarrh*, which does not differ in any essential from simple catarrh. The hyperemic mucous membrane may be rosy or livid, sometimes deepening into a brownish red. Occasionally the vocal cords appear dirty gray.

Large erosions are quite common. The vocal cords sometimes show loss of epithelium and sometimes hyperplasia of the epithelium. *Mucous patches* are of rare occurrence in the larynx. They are usually seen upon the free edges of the epiglottis, over the cartilages of Santorini, the arytenoid cartilage, or in the aryteno-epiglottidian fold. Lewin finds them most common in the middle of the vocal cords. They occur as rounded or oval, grayish-white spots, consisting of thickened and infiltrated epithelium, which do not project very considerably from the surrounding reddened tissues. When the epithelium is desquamated, the patch loses its grayish color and appears reddish and more like an erosion.

Inflammatory infiltrations, consisting of small round-cells, are of common occurrence in syphilis. They usually appear upon the vocal cords, epiglottis, and posterior walls of the larynx, where they form homogeneous thickenings, which sometimes slightly alter the form of the part.

The *gumma* of the larynx has no point of election. It is usually situated in some vascular tissue, as the submucosa. When multiple, gummata appear as round, sharply circumscribed, slightly projecting nodules of shot or pea size, sometimes lying so close to one another as almost to fuse. The single gummata occur as large circumscribed nodes with smooth surfaces. The inflammatory infiltration and gumma soften and ulcerate, with the formation of irregular lesions, the borders of which are flat or slightly swollen, rarely undermined, and surrounded by a marked hyperemic area. The base of the ulcer usually presents a creamy coating, upon removal of which a peculiar white, somewhat tough, firm, infiltrated tissue appears. The ulcers are more prone to deep erosion than to superficial extension, and not infrequently invade the cartilages, with the production of *perichondritis* and *necrosis*. The ulcerations following gumma are more circumscribed than those following cellular infiltration, and present very much the appearance of tissue having been cut out with a punch. When perichondritis follows syphilitic ulceration, it is apt to be severe and destructive; not infrequently abscesses form, with fistulous communications and extensions. Wide-spread caries of the cartilages and occasional exfoliation and expulsion of fragments or whole cartilages are seen. Gottstein says that perichondritis occasionally occurs without lesions of the mucous membrane, and that lesions of the mucous membranes may depend upon abscess formation and rupture.

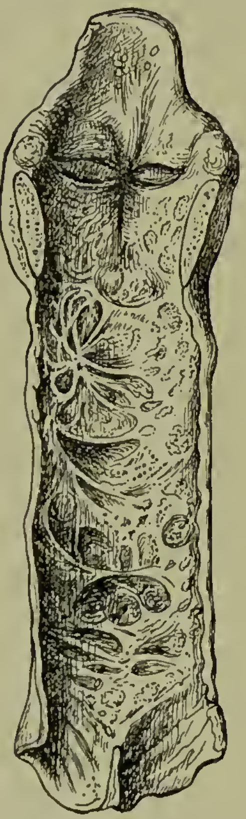

FIG. 265.—Syphilitic scars of the larynx and trachea (Orth).

The most serious thing about syphilitic laryngitis is the subsequent formation of *cicatrices*. These scars consist of dense cicatricial tissue, are usually stellate in appearance, and almost invariably contract, the contraction causing prominent projection of the cicatricial bands as ridges, which here and there cross the surface of the organ. Should such cicatricial tissue involve the vocal cords, or by their contraction pull upon the smaller cartilages, the form of the larynx may be changed, the deformity being sufficient to interfere with its proper function.

A characteristic of the syphilitic scars, first pointed out by Virchow, is that they are not productive in the center, though the edges are firm and callous. In the healing of the syphilitic ulcers it occasionally happens that small fragments of comparatively healthy mucous membrane irregularly project from their borders. These may take on a subsequent growth suggestive of hard papilloma. The ulcerations usually occur upon the epiglottis, vocal cords, and posterior walls of the larynx. The extension of the lesions may be such as completely to destroy the parts of the larynx affected. Fortunately, all cases do not continue unrestrained, and it is common to find the gummata and round-cell infiltration absorbed without ulceration, and the ulcers cicatrized without much destruction of the subjacent tissue.

6. **Lepra.**—The lesions of lepra are similar to those of syphilis, being characterized by the formation of nodules on the laryngeal mucous membrane. These nodules sometimes remain circumscribed and sometimes coalesce, producing irregular, thickened, nodular areas, resembling tuberculosis. They ulcerate with subsequent cicatrization. A characteristic which can be

used to differentiate syphilitic ulcerations from those of leprosy is the non-productive character of the central part of the cicatrix in the former.

7. **Glanders.**—Glanders of the larynx is a very rare affection in man. It is characterized by the formation of subepithelial cellular nodes, which invariably ulcerate and lead to the formation of larger and smaller denuded suppurating surfaces.

Tumors of the Larynx.—Polypi.—Polypi form an ill-defined group of morbid growths named from their shape, rather than from their histology. The majority of them are probably inflammatory in origin. They are common upon the vocal cords, and sometimes attain considerable size; occasionally they are cauliflower-like or dendritic, and are then spoken of as *condyloma acuminata*. They are composed of a fibrous framework covered with epithelium; there is usually more or less infiltration with small round-cells, and not infrequently a number of more or less dilated blood vessels. Such polypi or papillomata are most frequent in young people. By Sutton they are described as *laryngeal warts*, and are said to occur most frequently immediately beneath the vocal cords, and they not uncommonly occur beneath the attachment of the vocal cords to the thyroid cartilage. They may occur upon the ventricular bands and aryteno-epiglottic bands and even upon the epiglottis. Sometimes a single wart and at other times a dozen are present. Braus found 54 per cent. of 1100 cases of laryngeal tumors to be of this variety. Mulberry-like warts have occasionally been seen growing from the floor of the sinus pyriformis. Such polypi vary greatly in size, some being no larger than a pin-head, others as large as a cherry. They may be sessile or pedunculated, the length of the peduncle modifying the extent of their movability. When the peduncles are long, they are apt to get caught between the vocal cords and produce dyspnea that may terminate in asphyxia. They are usually pinkish in color; if hemorrhagic, red.

Fibromata form about from 8 to 10 per cent. of laryngeal tumors. They are usually sessile, and occur upon the vocal cords. They form small, smooth, rounded tumors.

Pedunculated fibromata vary in size from a lentil to a hazelnut. They not infrequently occur upon the vocal cords. **Lipoma, chondroma, myxoma,** and **adenoma** are of rare occurrence. The myxoma is said always to occur upon the vocal cords. The chondroma occurs in adults, and forms a smooth, rounded, sessile, immovable mass, which always extends inward. It may cause stenosis. The cartilage composing the tumor is hyaline.

Lipoma originates from the aryteno-epiglottic fold. Brases has reported an intralaryngeal lipoma.

Cysts sometimes occur from retention of the secretion of the mucous gland. They are most common upon the epiglottis and in the ventricles of the larynx.

Sarcoma of the larynx is not common. It may occur on the vocal cords, ventricular bands, ventricles, and epiglottis. It is usually unilateral, and is occasionally a pedunculated tumor. Mackenzie has collected 9 cases of spindle-cell sarcoma which originated from the tissues of the epiglottis. The tumor may assume a variety of external appearances, colors, and consistence. When large and sessile, the tumors are smooth, though occasionally warty in appearance and lobulated. The color is pink, meat-red, or dark red, sometimes yellowish or grayish. Both the round-cell and spindle-cell sarcomata occur. The tumors usually confine themselves to the laryngeal cavity, and in the course of a couple of months begin to spread. They do not affect the cervical glands, as a rule, thus differing from carcinoma.

Lymphosarcoma of the mucous membrane is rare.

Cavernous angiomata are of very rare occurrence in the larynx, and are seen in adult life. They spring from the vocal cords, ventricular bands, epiglottis, hyoid fossa, and lingual sinus. The tumors are generally sessile, but occasionally pedunculated. They may be bright red or purple in color. The surface is sometimes smooth, sometimes mulberry-like. They are rarely larger than a small bean. According to Sutton, the color of the tumor is its most striking clinical feature.

Holt reports a pedunculated lipoma of the arytenoid epiglottic fold and side of the epiglottis which extended into the esophagus for a distance of 22½ centimeters. It consisted of fat covered with mucous membrane.

Secondary epithelial tumors of the larynx are rare.

Epithelioma.—Sutton speaks of intrinsic and extrinsic epitheliomata in the larynx, the former arising from the mucous membrane of the vocal cords, ventricles, and ventricular bands; the latter from the aryteno-epiglottidian folds, the membrane covering the arytenoid cartilages, and the interarytenoid folds.

The *intrinsic form* usually begins in one of the ventricles, and is warty. The tumor sometimes takes on a papillomatous appearance, but in cases in which it is difficult to differentiate it from the simple wart it should be remembered that epithelioma is an affection of adults who have passed the meridian of life. Sutton regards any wart-like growth in an individual over forty years of age as suspicious. The tumor usually grows rapidly, life rarely being prolonged beyond two years.

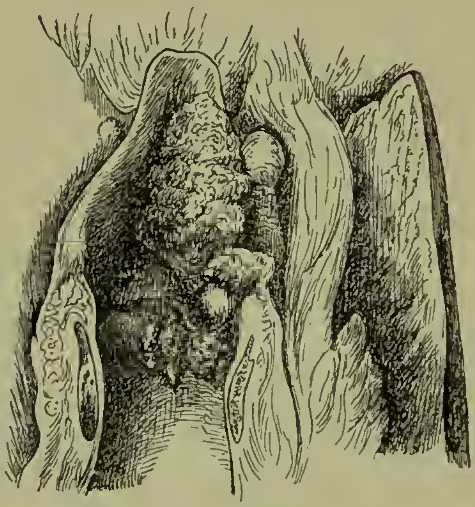

FIG. 266.—Papillary carcinoma of the larynx (Orth).

The *extrinsic form* is more formidable, in that it extends much more rapidly and infects the lymphatic glands at an earlier period. True carcinoma—that is, glandular cancer—may develop from the mucous glands of the larynx, but the majority of cases develop from the lining epithelium, and probably have their origin in simple warts.

Gottstein describes both a *medullary* and a *scirrhous form*, of which the one is hard and the other soft. The epithelioma he describes as a circumscribed, hemispheric, warty, cauliflower-like or coarsely tuberculated tumor of varying size and shape, which develops in the interior of the larynx. There can be no doubt but that this description refers to squamous epithelioma.

Histologically, the epithelioma of the larynx has no essential peculiarities.

Diseases of the Cartilages of the Larynx.—**Calcification of the cartilages** of the larynx is common in senility and in chronic inflammation. Most of the diseases of the cartilages are secondary to primary affections already pointed out. When inflammatory in nature, they depend upon tuberculosis, syphilis, phlegmons, etc., by which the cartilages are exposed and the way opened for inflammation.

Perichondritic abscesses are worthy of special consideration, because their rupture into the larynx is occasionally followed by secondary inflammation of the bronchial tubes and lungs. In marasmus and in the bedridden it sometimes happens that the pressure of the larynx upon the vertebral column brings about *necrosis* of the posterior part of the cricoid cartilage. The outcome of the severer forms of the cartilaginous diseases is almost invariably necrosis with exfoliation of the diseased tissue, sometimes of very minute portions of the cartilage, sometimes of entire cartilages.

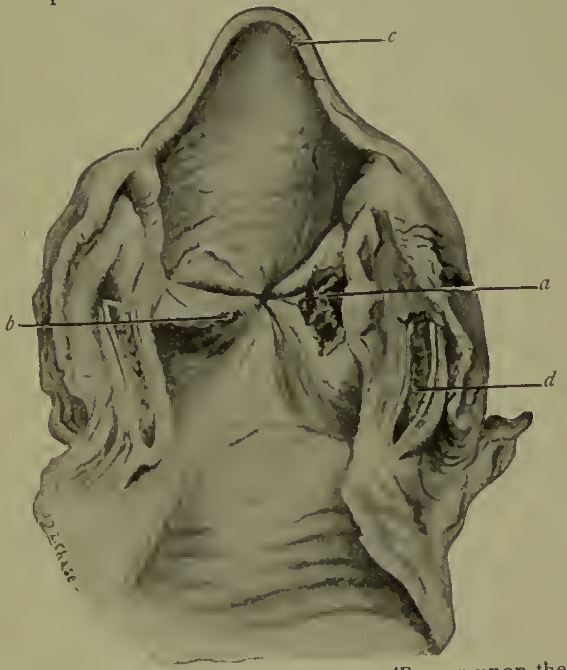

FIG. 267.—Squamous epithelioma of the larynx: *a*, Tumor upon the vocal cord and contiguous tissue; *b*, ulceration upon opposite side of larynx. This ulceration was caused by contact with the tumor; *c*, epiglottis; *d*, section through the posterior part of the thyroid cartilage.

DISEASES OF THE TRACHEA.

Inflammations.—These may be catarrhal, fibrinous, diphtheritic, mycotic, and ulcerative. According to their course, they may be acute or chronic.

Trachitis, or simple inflammation of the trachea, has no essential peculiarities. It is usually a secondary infection, depending upon diseased conditions of the larynx or bronchi, or a part of such general diseases as measles, variola, influenza, syphilis, whooping-cough, etc. *Diphtheritic trachitis* is rare. The condition is usually characterized by simple redness, with slight swelling of the mucous membrane, depending upon increased vascularity and hypersecretion. In traumatic lesions produced by the inhalation of irrespirable substances the trachea may also suffer, but the brunt of the injury is sustained by the larynx. The *necrotic form* is rare, and results from the intratracheal growth of aspergillus, leptothrix, etc.

Tuberculosis.—Primary tuberculosis of the trachea seems to be exceedingly rare. The majority of cases depend upon secondary infection from primary diseases of the lungs. The lesions usually appear as small, isolated, miliary tubercles or tuberculous ulcers. If these attain sufficient size and extend deeply enough, the cartilaginous tissue may be invaded and destroyed.

Syphilis.—Syphilitic trachitis is rare. The upper part of the trachea not infrequently suffers from an invasion of the lesions from the larynx. Gumma, however, may occur in the larynx and trachea as well, and by softening, produce the characteristic ulceration followed by stellate cicatrices, which contract and narrow the lumen of the tube.

Tumors.—**Fibroma, sarcoma, chondroma, osteoma, adenoma,** and **carcinoma,** together with various secondary tumors, have been described. The secondary tumors most commonly originate in the thyroid gland.

Primary carcinoma of the trachea may occur from the epithelial cells of the mucous glands.

Secondary epithelioma from primary tumors of the esophagus is not common.

Cysts.—These are occasionally seen on the posterior wall of the tube, and sometimes attain the size of a hazelnut or walnut; they usually project outward between the trachea and the esophagus, and probably depend upon obstruction of the mucous glands.

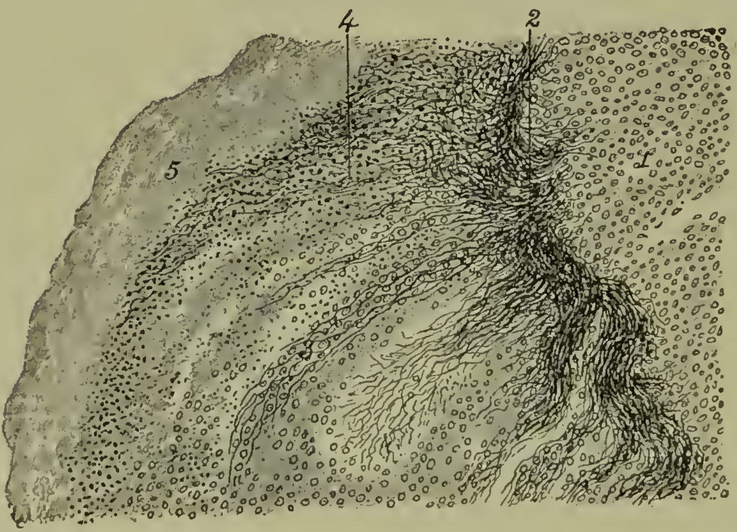

FIG. 268.—Diphtheria of the trachea (Weigert's fibrin stain): 1, Infiltrated tissue of the tunica propria; 2, fibrin layer covering the largely necrotic mucous membrane; 3, remains of epithelium; 4, peripheral layer of the diphtheric pseudomembrane, consisting of nuclear fragments and leukocytes; 5, non-nucleated necrotic masses (× 130) (Dürck).

DISEASES OF THE BRONCHI.

Bronchitis.—This is the most common affection of the bronchial tubes, as well as one of the most common of the respiratory apparatus. It is generally an acute catarrhal inflammation of unknown origin, affecting the mucous membrane of the bronchi, and characterized by a marked congestion with an accompanying mucous, serous, purulent, mixed, or fibrinous exudate. The mucous membrane appears bright red or purple, thick, opaque, and velvety. The mucus, which is secreted in considerable quantities, is derived from the much-enlarged mucous glands and also from goblet cells, of which the mucous membrane furnishes a large number.

Swelling of the mucosa diminishes the caliber of the tubes and causes dyspnea and accelerated breathing.

Etiology.—The etiology of bronchitis is obscure. Popular experience sanctions the belief that it depends upon exposure to cold. Some believe it to be due to a *paralysis of the blood vessels caused by cold.* It may follow the inhalation of hot or cold air or irrespirable gases. The fact that the affection is ushered in with malaise, aching in the bones, a sense of constriction of the chest, etc., might indicate that intoxication has something to do with it. On the other hand, the fact that many cases begin with coryza and successively suffer from pharyngitis, laryngitis, trachitis, and bronchitis, suggests that it is a specific process with a progressive invasion. Bergey thinks it depends upon bacteria regularly present in the respiratory passages. No specific bacterium has been found.

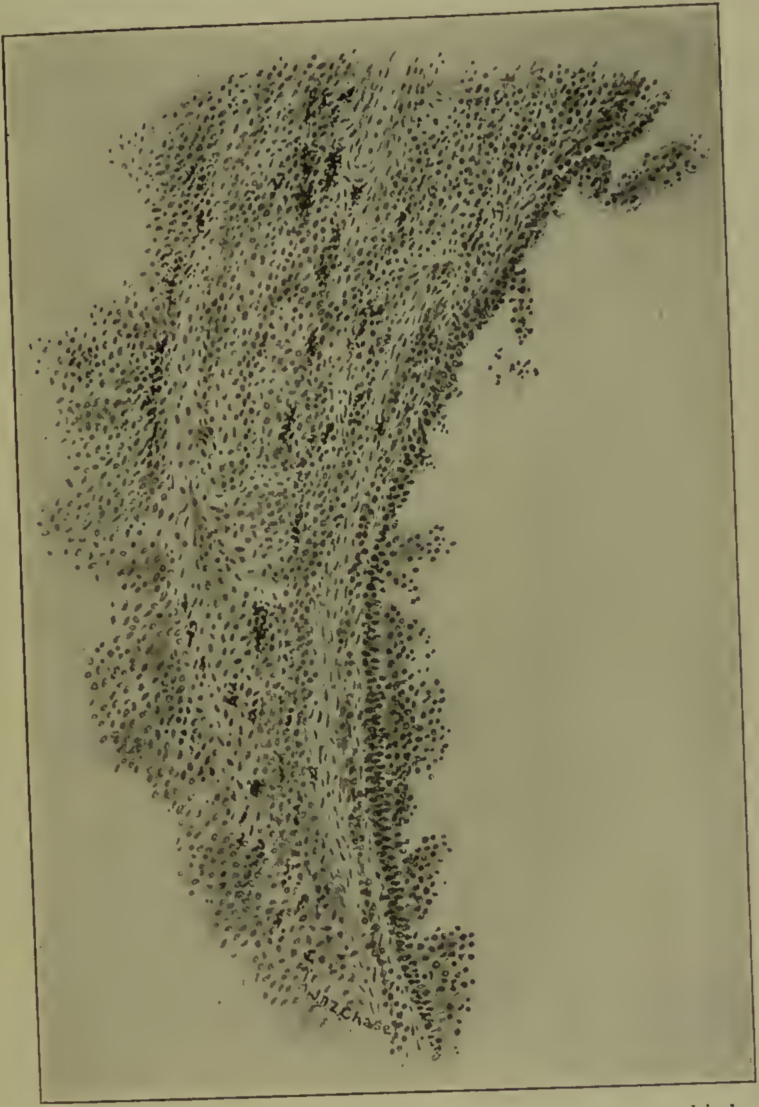

FIG. 269.—Bronchiectasis. Section through a greatly dilated and atrophic bronchial tube. The mucous lining is present, though in a state of catarrhal inflammation. The wall of the tube is supported by indurated pulmonary tissue (Oc. 4; Ob. 3).

Ziegler describes two forms of bronchitis: *bronchorrhœa serosa*, in which the expectoration is serous in character; *bronchoblennorrhea*, in which the secretion is purulent. A fetid secretion usually depends upon the entrance of putrefactive bacteria. The disease is a very simple one, and characterized chiefly, as seen at autopsy, by redness and increased secretion. Should the bronchial walls be examined microscopically, however, multiplication and desquamation of the epithelial cells, copious formation of goblet cells, and a moderate amount of cellular infiltration of the subepithelial tissues may be observed. In severe cases, depending upon local infection of the deeper portions of the lung, the inflammatory process sometimes extends through all the thickness of the tube to the surrounding pulmonary tissues. The disease readily recovers. When of prolonged duration, it is likely to be followed by atrophy of the bronchial walls, considerable relaxation, and occasional localized hyperplasia.

Bronchiectasis.—Protracted cases of bronchitis may lead to atrophy and relaxation of the tubes, which in turn predispose to dilatation. Such dilatations were described by Laennec as *bronchiectases*. They are most commonly seen in the lower and middle lobes of the right lung, and are either cylindric, fusiform, or saccular in shape. They are most common in tubes of the second and third subdivisions. There may be one dilatation upon a single bronchus, or many of the tubes may show them. Different forms may occur at the same time, and atrophy of the intervening tissue may cause neighboring dilatations to communicate.

Etiology.—The etiology of bronchiectasis can probably be summed up in—(1) Increased air-pressure from chronic bronchitis with cough. (2) Relaxation of the tissues depending upon inflammation. (3) Pressure of stagnating secretions. (4) Traction on the bronchial walls by cicatricial bands in the lung.

The cause of the bronchiectasis is, no doubt, the pressure of the air upon the yielding vessel-wall. If the yielding be uniform, a cylindric dilatation results, but if it is irregular because of local disease of the vessel-wall, a saccular dilatation results. There is but slight anatomic alteration of the tube. Laennec described dilatations with thickening, without thickening, and with thinning of the walls. In rare instances the cartilaginous plates disappear and are replaced solely by connective tissue. Laennec believed that bronchial catarrh was the exciting cause of the dilatations.

It sometimes happens that when the entrance of air into one lung is prevented and an excess is, in consequence, thrown into the other, the pressure of the air within the bronchi becomes greater than they can stand, and dilatation of the tubes results. Grawitz has seen a case of *congenital bronchiectasis*. Occasionally the shrinkage of the surrounding lung tissue, as in cases of fibroid phthisis, operates upon the bronchial tubes in such a way as to stretch them and increase their lumen.

Retained secretions that collect in the lumen of the bronchus usually cause saccular, but occasionally cylindric, dilatations. When numerous, the saccular dilatations may be arranged along the length of a tube like beads on a string. Numerous bronchiectatic dilatations give a section of the lung tissue, especially when indurated, the appearance of being full of holes. The retention of secretion within the cavities sometimes causes the formation of cysts.

The mucous membrane undergoes marked atrophic changes similar to those seen in chronic bronchitis. The epithelial layer loses its cells, and the submucous tissue undergoes a marked connective-tissue hyperplasia.

Ulcerations of the bronchial vessels sometimes follow acute and chronic inflammations, sometimes depend upon the entrance of foreign bodies into the tubes. The most common causes, however, are tuberculosis, syphilis.

and epithelioma. The ulcerations may be superficial, destroying more than the mucous membrane, or may be deep and lead to necrosis of the cartilages or perforation of the bronchial tube. Through the perforation thus formed purulent or mucopurulent secretion of infectious nature can escape into the parenchyma of the lung, where inflammatory infiltration, necrosis, caseation, and suppuration may occur, according to the nature of the infection. Secondary infections of the surrounding tissue are described as *peribronchitis*, and cavities may be formed in the lung tissue by their erosion.

Cavities of this kind are not infrequent in tuberculosis, the wall of the cavity consisting of infiltrated, consolidated, gangrenous, or cheesy lung tissue. The contents of the cavity vary according to its formation—in cases of gangrene consisting of fetid material; in cases of tuberculosis, of soft, cheesy, or creamy pus; and in more simple infections, of mucopurulent matter. Occasionally the bronchial tubes are perforated from without, especially in pulmonary tuberculosis with enlargement of the bronchial glands

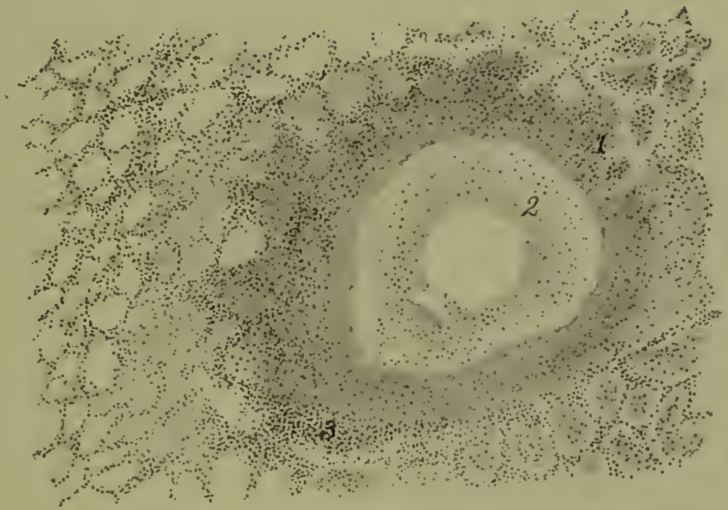

FIG. 270.—Caseous bronchitis. Transverse section through a small bronchus and surrounding lung tissue. The wall of the bronchus is completely broken down, caseated (1), its lumen partly filled with the cheesy material (2). The tuberculous process extends in a circular manner outward to the surrounding lung tissue; the alveoli of the latter are infiltrated and filled with numerous confluent tubercles (3) (× 40) (Dürck).

and pressure upon the bronchial tubes. Aneurysms sometimes press against the bronchial tubes, and lead to atrophy and perforation.

Birch-Hirschfeld restricts the term bronchitis to inflammation of the larger tubes, and prefers to use the term *bronchiolitis* for inflammation of the tubes below the third or fourth bifurcation. Inflammation of these bronchioles does not differ from inflammation of the larger tubes, except that the thinness of the walls facilitates the spread of the inflammation from the tubule to the surrounding tissue, and thereby occasions a frequent combination of inflammation of the tubule and surrounding tissue, a condition described as *bronchopneumonia* or *peribronchial pneumonia*.

While bronchiolitis is not easily differentiated from bronchitis anatomically, the two affections are quite different clinically. Bronchiolitis is usually a primary affection of the larger tubes observed in extremes of life—infancy and old age. It is frequently accompanied by bronchopneumonia.

Fibrinous Bronchitis.—True diphtheria of the bronchi is very rare, and is usually secondary to diphtheria of the larynx. A non-diphtheritic croupous or fibrinous bronchitis may occur in croupous pneumonia and in streptococcus infection. The infected tubes are reddened and inflamed and covered with a grayish or grayish-yellow pseudomembrane.

The term fibrinous bronchitis usually refers, however, to a quite different affection, characterized by the infrequent occurrence of violent attacks of cough, followed by the expectoration of a peculiar, firm, coherent and fibrinous, dendritic mass, corresponding to the small bronchial tube with its minute ramifications. The disease begins with catarrhal bronchitis, more rarely with sudden dyspnea and fever. In a few days the characteristic fragments occur in the expectoration. It is said that in very severe cases the obstruction of the smaller branches of the bronchial tree by this coherent mass may lead to death from asphyxia. The larger end of the expectorated mass corresponding to the largest of the tubes is usually hollow ; the smaller parts, solid. The structure is frequently stratified. The color varies from yellowish-gray to reddish. Charcot-Leyden crystals are common in the mass, and Curschmann's spirals not infrequently occur at the termination of the finest branches of the coagulum. The epithelium of the tube is sometimes detached with the cast. Neelson found that the material forming these branched masses is not fibrin, not answering to the reactions for fibrin, but inspissated mucus.

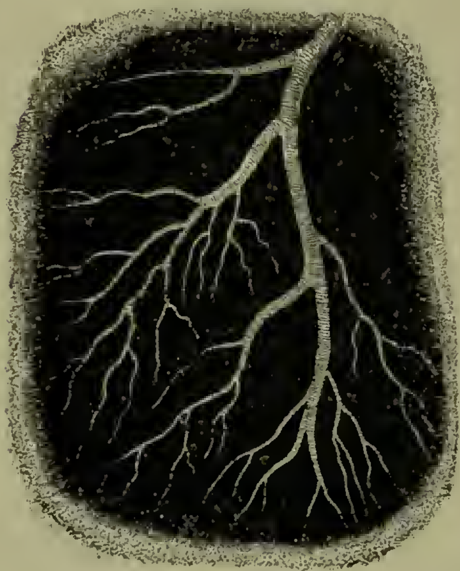

FIG. 271.—Large bronchial coagulum ; chronic fibrinous bronchitis (Vierordt).

Syphilis of the bronchial vessels is a very rare affection, and has no essential peculiarities, the lesions resembling those seen in the larynx and trachea. In rare cases in which gumma forms, it may be impossible to distinguish between gumma of the bronchus and gumma of the lung.

Tuberculosis of the bronchial tubes is one of the most constant, if not invariable, accompaniments of pulmonary tuberculosis. It usually occurs in the smaller vessels in the neighborhood of the tuberculous tissue, but from any primary focus may extend along the tube in the peribronchial lymphatic tissue. Probably the usual mode of infection is from the lumen of the tube, through infectious matter which it contains. Especially is this true in cases in which there are cavities in the lung, or in which there are softened pulmonary tissues, from which purulent material containing tubercle bacilli enters the bronchial vessels. The lesion usually begins with the formation of small gray tubercles projecting slightly from the surface, and tending to increase in size and number, caseate and ulcerate, leading to the formation of excavated ulcers, the borders and base of which consist of necrotic, whitish, softened material. In the histologic study of the bronchial vessels one must remember that they contain scattered collections of lymphoid tissue, which must not be mistaken for tubercles.

In any diseased condition in which the bronchial vessels are the seat of inflammatory infiltration there is always danger that the collection of secretions upon the surface and in the lumen of the tube may obstruct it. Such obstructions are temporary, as a rule, and disappear with the removal of the cause, which is either absorbed or expectorated. If, however, the obstruction should be of such a nature that its removal is impossible or accomplished with great slowness, permanent obstruction may follow. The most common cause of permanent obstruction and obliteration of the smaller bronchial tubules is tuberculosis of the lung. Ziegler states that it is possible to find obliterated bronchioles in every tuberculous lung.

The contents of these obliterated bronchioles is usually caseous, so that a section which passes through them appears to sever a rounded, encapsulated, caseous node, the contents of which may be sharply defined or may merge into its capsule.

When retained secretions from old catarrhal affections of the lungs cause permanent obstruction of a more benign nature, one sometimes finds lime-salts deposited in the secretion, causing a true bronchial calculus (*bronchiolith*). Obstruction of the bronchial tubes also sometimes follows the entrance of foreign bodies, and may result from the contraction of scars. Retained foreign bodies cause bronchitis, and may lead to saccular bronchiectasis. Deposition of lime-salts upon them changes them to bronchioliths. It also sometimes happens that the pressure of aneurysms, neoplasms, and other external growths may cause more or less complete and permanent obstruction.

Following chronic bronchitis of any kind, perhaps more often in those forms in which plugs of retained secretions occur in the lung, one finds an increase in the amount of connective tissue surrounding the bronchial vessels, leading to *fibrous peribronchitis*. Ziegler divides bronchitis into *endobronchitis*, the usual form, *mesobronchitis*, the chronic form, in which, together with inflammation of the lining membrane, there is an increased production of connective tissue in the deeper coat, and *peribronchitis*, in which the inflammation is altogether without the vessel, and is sometimes associated with peribronchial lymphangitis. All the conditions may succeed the first, or all may occur together, or they may occur in the reversed order, as in cases in which inflammations of the pleura have extended along the interlobular septa to the peribronchial connective tissue.

Tumors of the Bronchi.—**Polypi** sometimes occur as the result of chronic catarrh. They consist chiefly of outgrowths of mucous membrane, which, no doubt, have originated as small villosities at the edges of cicatrized ulcers. **Lipoma** has occasionally been seen. Birch-Hirschfeld has reported three cases of the small round-cell **sarcoma** of the larger bronchial branches. Bronchial cancer is rare; it usually has its point of origin in the branches of the second or third order, and is confined to one lobe of the lung—more commonly the lower lobe. On examination the tumor appears as a medullary, soft infiltration of the bronchial wall, in which the layers are gradually lost.

DISEASES OF THE LUNGS.

1. DISEASES DEPENDING UPON ABNORMALITIES IN THE DISTRIBUTION OF THE AIR.

Atelectasis or collapse of the lung may be:

(*a*) **Congenital.**—This is sometimes spoken of as *apneumatosis*. Fetuses always have solid and unexpanded lungs resembling liver tissue; the entrance of air with the first inspirations causes an entire change in their appearance. Failure of expansion of any part of a lung is *fetal atelectasis*.

Etiology.—There may be various causes: thus, a bronchus may be closed from obstructing mucus or meconium, or the lung may be pressed upon or diseased, or there may be insufficient respiratory energy, especially in prematurely born children. Atelectasis depending upon obstruction is spoken of by clinicians as *obstruction atelectasis*.

(*b*) **Acquired.**—Atelectasis is acquired when it develops after the lungs have once been fully expanded.

Etiology.—The lung may be compressed by pleuritic effusions, pneumothorax, upward pressure of the diaphragm, from diseases of the abdomen, deformities of the spinal column, neoplasms, etc.; or a bronchus may be plugged by inspired foreign bodies or secretions, and the air subsequently absorbed, so that the air-cells collapse. The lung tissue appears pale-red, violet, purplish-gray, or brownish in color, and is tough, hard, dry, empty of air, and does not crepitate. Fragments of the tissue sink in water. When the collapse is recent, the lung may sometimes be artificially expanded during life by blowing into the windpipe, or after death by inflating the bronchial tubes. When the condition has persisted for a considerable length of time, it is quite usual for congestion of the tissue to take place, and the lung to appear of a darker color and peculiar consistence, described by the term *carnification.* This condition leads in its turn to a still more altered appearance, known as *splenization,* in which there is proliferation of the connective tissue, the tissue having the color and consistence of splenic substance. In cases of extreme weakness from phthisis, typhoid, nervous diseases, etc., in which the body maintains the same position for a long time, a *marasmatic atelectasis* may develop. Obstructive atelectasis is the most common form, its most frequent cause being inflammation of the bronchioles. It occurs in irregularly distributed patches, which cause the lung to present upon its surface alternating patches, dark bluish red, pale red, or grayish in color, in marked contrast to the pink-white or grayish color of the normal lung tissue.

When an atelectatic area remains from infancy to adult life, its appearance is that of a depressed, perfectly white area, covered with thickened pleura, which not infrequently rubs upon a thickened parietal pleura. When incised, it is found to contain numerous bronchiectatic dilatations, some of which are empty, others filled with inspissated mucus. The bronchial openings are for the most part tubes which pass through the atelectatic area on their way to the normal tissue beyond. When examined microscopically, the tissue appears highly vascular, entirely free of pigment, and resembles fetal lung. Epithelial cells are found in some of the alveoli. The local areas are most frequently observed upon the base of the left upper lobe, middle right lobe, and posterior part of both lower lobes

Emphysema, or pulmonary inflation, is a condition in which the lung contains an abnormally great amount of air. It is important to differentiate between it and simple pulmonary inflation, such as follows obstruction to the flow of air into central parts of the lung, and allows its excessive entrance into other parts. This is usually a temporary matter, and not particularly serious. Birch-Hirschfeld includes as emphysema only such cases as present a histologic alteration of the alveolar walls. To the pulmonary inflation caused by forced inspiration clinicians have applied the term *acute vesicular emphysema.* The air-cells are not altered in structure, but are simply dilated beyond their usual capacity.

Etiology.—The most common cause is bronchopneumonia. The distended lobules are pale, spongy, and anemic, and project beyond the surface of the lungs.

When the pressure of the air is great, the air-cells sometimes burst and allow the air to escape into the interstitial pulmonary tissues. This is spoken of as *interstitial, intervesicular,* or *interlobular emphysema.* It occurs in consequence of violent cough in bronchitis or bronchopneumonia. The escaped air outside of the alveoli may compress and occlude them and lead to death from asphyxia. Ordinarily the condition is not very serious, and the number of air-cells that rupture is very small. The ruptures usually occur on the interior surface of the upper lobe of the lung, and the air usually escapes so as to form little bladders varying in size from a pin-head to a chestnut. These little bladders sometimes travel along from the point of origin to the hilus of the lung, and the air occasionally enters into the areolar tissue of the mediastinum.

Chronic, substantial, idiopathic, or **diffuse emphysema** is usually found in persons who suffer from chronic bronchial catarrh, or whose occupations interfere with the free entrance and exit of air from the lungs. A few individuals seem hereditarily predisposed to it. The disease is characterized by great enlargement and distention of the lungs. Both lungs are affected, and usually equally so. The edges are particularly inflated and rounded. At the base of the lung one very often finds groups of enormously distended lobules forming distinct air-bladders. The lungs are unusually pale in color; when the chest is opened, they do not readily collapse, and, therefore, are less elastic than normal. When emptied of air, they are small, very soft and flabby, and the edges are almost membranous.

When the tissue is examined microscopically, one cannot fail to be struck by the enormous size of the air-cells, which are not only distended, but have lost many of the interalveolar septa, so that neighboring air-cells unite and form abnormally large cavities. With the loss of the interalveolar septa the capillary surfaces are much reduced, and the oxygenation of the blood greatly lessened.

Etiology.—Numerous theories have been suggested to explain idiopathic emphysema, of which none is perfectly satisfactory. Three of these are usually mentioned:

1. The inspiration theory teaches that the air-cells become overdistended with air in consequence of diminished expiratory force, due to loss of elasticity of the lungs and chest.

2. The expiratory theory explains the changes by presuming that the apices, margins, and edges of the lung are dilated when the escape of air from them is prevented by a partially closed glottis, etc., during cough, straining at stool, lifting, etc.

3. The nutritive theory teaches that the disease depends upon histologic changes in the interalveolar septa, which lose their elastic tissue and then can no longer contract to expel the air.

Most likely it depends upon an interference with the exit of air from the lungs; thus, it is found in those who play wind-instruments in bands and especially such instruments as require forcible blasts of air; and among glass-blowers, who make deep inspirations and expire against considerable resistance. The same condition may be operative in cases of chronic catarrh of the lung, in which the patient inspires deeply and then expires violently against secretions which partially interfere with the escape of the air, and which he hopes to discharge by expectoration. In both conditions there is a preliminary inspiration of unusual depth, but whether it is this or the forcible expiration against resistance that brings about the distention, it is difficult to say. A partial key to the matter is offered by observing the local areas of emphysema, which occur in bronchial catarrh and seem in many cases to be the result of a difficult expiration on account of tenacious secretions within the bronchioles.

In many cases emphysema seems to follow such disturbances of nutrition as marasmus and senility. The atrophy of the alveolar wall begins where it is thinnest, and is accompanied by separation and disappearance of the elastic fibers. Grawitz thought that these fibers were transformed into cells, the change leading to diminished resistance of the alveolar walls. Small openings soon appear between neighboring alveoli, becoming larger, leading to stretching and ultimate destruction of the capillary vessels. The epithelium is passive. It sometimes undergoes fatty degeneration. When, from any cause, portions of the lung become atelectatic or consolidated, the acute vesicular emphysema may become a permanent, local condition, characterized by all the peculiarities of the substantial emphysema. It is then sometimes spoken of as *vicarious* or *compensatory emphysema*. It is sometimes lobar, sometimes lobular, in distribution. The marasmatic form of emphysema occurring in old age is spoken of as *senile emphysema*. Brown and Stahel, finding that the large bronchi become considerably dilated, have established a rule that in unilateral vicarious emphysema the distention of the lung is proportionate to the transverse diameter of the conducting air-tube.

It is interesting to note that emphysematous tissues are free from the ordinary pigmentation so common in the lungs of those exposed to soot and dusts. Various explanations have been offered why this should be the case, Birch-Hirschfeld probably coming nearest the truth in thinking that with the atrophy of the alveolar walls the pigment is liberated and expectorated, while the remaining portions are carried away by wandering cells.

The substantial emphysema is characterized by a peculiar deformity of the chest, which assumes a barrel shape. The loss of capillary surface also greatly impedes the pulmonary circulation, and causes a general engorgement of the venous system, with various secondary changes in the abdominal and circulatory organs.

2. DISEASES RESULTING FROM ABNORMALITIES IN THE PULMONARY CIRCULATION.

Simple acute congestion of the lung is probably a very common condition, and one that usually causes little solicitation. It may, however, be serious and even fatal. In occurs in consequence of the inhalation of irritating gases, hot or cold air, or may result from the irritation of substances circulating in the blood. It may also be collateral, occurring in one part of the lung because of obstruction elsewhere, and may be the precursor of various inflammatory conditions of the lung. It is well known clinically as the *stage of congestion* in croupous pneumonia. It may be local or common to the entire lung or to both lungs, and is a transitory condition in which the lung presents no other changes than vascular engorgement and a small amount of intravesicular exudation.

In rare cases pulmonary congestion is fatal, and upon postmortem examination the lung appears increased in size, dark red in color, denser than normal, and unusually poor in air. When incised, frothy blood is easily expressed. The lung tissue readily floats upon water.

Chronic Congestion of the Lung or Passive Hyperemia.—This usually occurs in cases in which the escape of blood from the pulmonary veins is prevented, or when the force of the heart is weakened. The condition is bilateral and generally uniform.

It occurs in cases of heart disease, in cerebral injuries, and in various asthenic and adynamic conditions. It is one of the most frequent lesions found *postmortem*. The most common lesions with which it is associated are insufficiency and stenosis of the mitral valve and aortic obstruction. The lung is dark blue in color and feels solid; crepitation is diminished. When incised and pressed, a dark-reddish or purplish fluid or a somewhat frothy, hemorrhagic fluid escapes. The passive congestion that occurs in adynamia is usually situated in the posterior inferior portions of the lung,—that is, in the dependent portions,—and probably depends upon the general weakness and relaxation of the vessel-walls. It is called *hypostatic congestion*. When the chronic congestion has existed for a long time, the lung tissue becomes unusually dense and firm—congestive induration from hyperplasia of both the fibrous and elastic tissues.

Inasmuch as this condition of pigmentation is usually associated with an induration and reduction in size, resulting from the passive hyperemia and connective-tissue proliferation and contraction, it is generally described as *brown induration* of the lung. The lungs vary from a salmon-pink to a brownish-red color, and are mottled with brown or black spots. They may be dense and firm, or edematous or splenized. In most chronic heart affections associated with chronic congestion of the lung these pigmented cells are of almost constant occurrence in the sputum, and have been spoken of by German writers as *Herzfehlerzellen*. Brown induration is most common in mitral disease.

Hypostatic congestion predisposes to infection and not infrequently leads to hypostatic pneumonia, especially in typhoid fever and other adynamic conditions.

The histology of passive congestion is simple. The vessels of the lung are dilated, the mucous membrane swollen and injected, the interstices of the interalveolar tissue distended with fluid, and the air-cells filled with a small amount of slightly hemorrhagic exudate. The condition is on the border-line of edema. Occasionally there may be minute extravasations of the blood, due to rupture of the smaller capillaries.

Anemia of the lung is a rare affection, and depends upon vascular obstruction from pressure, tumors, aneurysms, etc. One must bear in mind that immediately after death the tendency is for the blood to gravitate to the dependent portions of the organ, causing the upper part to appear bloodless and anemic.

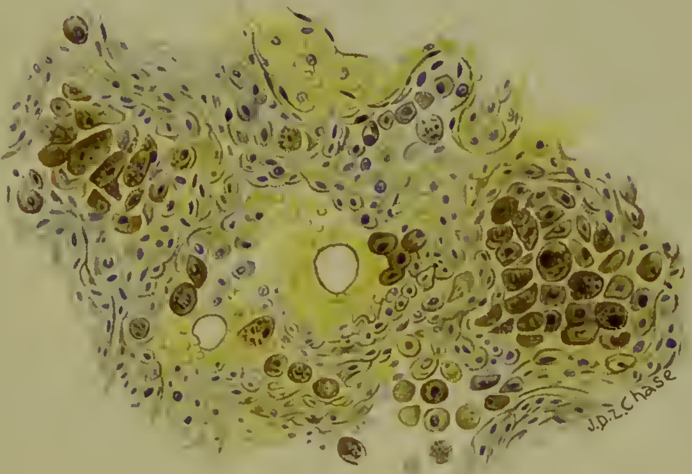

FIG. 272.—Brown induration of the lung from a case of obstructive heart disease, showing the air-cells occupied by desquamated epithelial cells pigmented with pigment (hemosiderin) from the destroyed red blood-corpuscles (× 240).

Edema of the lung is characterized by the escape of serous fluid into the air-spaces and tubes. It is a very common condition, and may depend upon diseases of the heart and vascular system; upon diseases of the kidneys; upon inflammatory conditions in the neighborhood of the chest; upon old age and debility. It may depend upon extremes and sudden changes of temperature, and upon inhalation of extremely hot or extremely cold air. A sudden change from an extremely hot to an extremely cold atmosphere may suddenly drive the blood from the surface of the body to the lungs, causing edema. In rare cases iced drinks taken at times when the body-temperature is high are said to have produced it. Diseases of the lungs themselves, such as emphysema, pneumonia, pleuritis, etc., have been known to bring about edema. Diseases of the liver, such as cirrhosis, abscess, and amyloid disease, Hodgkin's disease, leukemia, chlorosis, and various other anemias associated with hydremic blood, may cause it. Infectious diseases, such as acute rheumatism, certain obscure affections, such as diabetes, puerperal eclampsia, and acute spinal palsy, are sometimes accompanied by fatal edema of the lungs. Malignant diseases of the stomach and other organs sometimes cause edema of the lungs. It will be seen that many of these are terminal pulmonary edemas, and depend upon weakness of circulation and hydremic conditions of the blood, rather than any peculiarity of the diseases themselves. Angioneurotic edema also occurs in the lung, and depends upon vasomotor and trophic causes as yet not understood. Its peculiarity is a tendency to appear unexpectedly without any warning, the health of the patient usually being good. The attack may be ephemeral or may cause death.

Cohnheim believes that it depends upon obstruction or disease of the endothelium of the smaller vessels and capillaries, and Landerer that it depends upon relaxation of the vessel-walls. In septic and toxic conditions there may be hyaline degeneration of the vessel-wall. The inflammatory edemas, which depend upon inflammation of the lung tissue or neighboring tissues, differ from the ordinary edemas in having a pronounced catarrhal type, characterized by a marked desquamation of the pulmonary epithelium, an unusual amount of albuminous ingredients in the transuded fluid, and a greater admixture of blood.

Morbid Anatomy.—The condition is very common, and may affect both lungs, one lung, or only part of a lung. The lung tissue is pale and anemic, or dark and hyperemic, according to the amount of simultaneous congestion. It is probable that edema is of frequent occurrence at the moment of death agony, when the capillaries relax. *Macroscopically*, the lung appears unusually large, is pale, feels boggy to the touch, and is very heavy. When elevated, water can be seen descending along the bronchioles and distending the inferior parts. The surface is usually smooth and shining, and the whole organ unnaturally moist. It can be cut with ease, when more or less blood-stained serum mingled with froth at once escapes in considerable quantity. When pinched, it crepitates. When examined *microscopically*, one finds more or less pronounced hyperemia, and air-cells filled with a slightly albuminous fluid. The epithelial cells of the alveolar walls may be desquamated and the interstices of the interalveolar tissue are increased in size.

Ziegler points out that in specimens hardened in alcohol or Müller's fluid there is a granular precipitate of coagulated albumin. Occasionally, especially in the inflammatory edemas, leukocytes and fibrin may be found in the exudate.

Pulmonary Hemorrhage.

—Hemorrhage from the lung is called *hemoptysis*. It is a common accident.

Etiology.—It may depend upon a variety of causes, tuberculosis pulmonalis being the most common. It occurs also in hyperemia, ulceration, and traumatism of the lung from gunshot wounds of the chest, the rupture of intrathoracic or pulmonary aneurysms, gangrene of the lung, and hemophilia. It may also follow violent bodily exertion, such as heavy lifting, coughing, loud crying or singing, etc. It also occurs in croupous pneumonia, fibrinous bronchitis, emphysema, fibroid phthisis, syphilitic pneumonia, bloody edema, malignant disease, and embolism. Brown-Séquard has pointed out that in rare cases pulmonary hemorrhage follows cerebral apoplexy and brain tumors. In rare cases it also follows the inhalation of irrespirable substances, such as chlorin gas; and in still rarer cases, of which there are a few on record, as a result of vicarious menstruation. Diminished atmospheric pressure, as in the sudden ascent of high mountains, has occasionally brought on unexpected and severe hemoptysis. The amount of blood which escapes will vary according to the condition causing the hemorrhage. Thus, in hyperemic and inflammatory conditions, the expectorated blood is derived from the inflammatory exudate, which slowly escapes into the air-cells, and cannot be great in amount, while in the rupture of aneurysms and tuberculous erosion of large arteries the loss of blood may be so great as to be fatal. The blood is usually expectorated, but some is aspirated into the deeper portions of the lung during inspiration, and enters the healthy bronchioles and lobules, filling the air-cells and forming airless, hemorrhagic, blackish-red areas of considerable size. The lung tissue may thus become entirely consolidated from the displacement of its air, the dark-red, soft, blood-saturated tissue resembling the spleen in consistence. It is often spoken of as splenized. Hemorrhagic infarctions are local hemorrhagic areas.

When such infarcted or saturated areas are examined microscopically, the alveoli are found full of blood. The most common cause of intrapulmonary hemorrhage is infarction following embolism of the lung. The infarcted areas are usually situated beneath the pleura, are sharply circumscribed, and of a conic shape, the base being directed toward the pleura, and the apex toward the hilus of the lung. In the fresh condition they are of a blackish-red color, dense, and airless. The infarcts may be pea sized or as large as an egg. When fresh, the pleural covering is shining and unaltered. When older, however, the surface is usually covered with some fibrinous exudate.

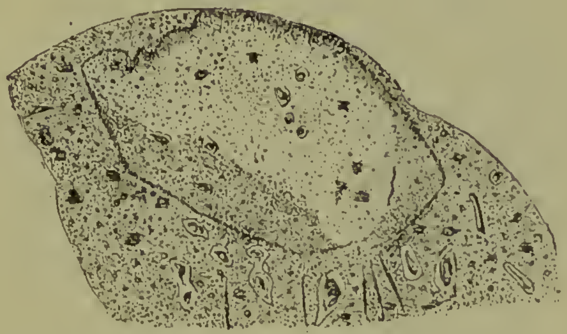

FIG. 273.—Irregularly wedge-shaped embolic hemorrhagic infarct in the lung, following thrombosis in the right auricle, in a woman with mitral stenosis. The border is sharp; the area, quite homogeneous and red (Hektoen).

Obstruction of the pulmonary circulation is not always followed by hemorrhagic infarction, as collateral circulation is easily established in the lung. After the infarct has existed for a short time, it becomes sharply differentiated from the surrounding healthy pulmonary tissue by reactive inflammation. When the infarct is small, so that the infiltrated tissue does not die, the integrity of the pulmonary tissue may be restored by resorption of the extravasate, a slightly indurated, pigmented area then remaining. In many cases the infarct is sufficiently large to destroy the vitality of the infiltrated tissue, under which circumstances, if no infection occurs, the healing takes place by reactive connective-tissue formation. The subsequent contraction of the cicatrix causes the infarcted area to appear as a deep pucker upon the surface of the pleura, with a fibrous node at its center. When the embolus is infectious in nature, suppuration or gangrene may take place in the infarcted area.

Gangrene of the Lung.—Etiology.—Gangrene of the lung invariably depends upon the entrance of bacteria into divitalized pulmonary tissue. A variety of lesions may make this possible. Thus, diseases of the lung itself, such as croupous pneumonia, tuberculosis, carcinoma, and embolism, may be followed by gangrene. Again, diseases of the upper respiratory passages by which fetid material enters the lung, such as gangrene of the larynx, the entrance of foreign bodies into the bronchi, and the extension of disease from neighboring organs, as in epithelioma of the esophagus with perforation into a bronchus. Some cases, called *idiopathic*, occur in alcoholism and asthenia from undiscoverable causes, probably primary infections.

Morbid Anatomy.—Since the days of Laennec it has been customary to divide the lesions into the *diffuse* and *circumscribed*. The circumscribed form occurs in irregularly rounded single or multiple areas, which on transverse section show a dark-brownish, greenish, or blackish color. They are dry and surrounded by hyperemia and edema. Should such a gangrenous area extend to the pleura, a rich, fibrinous deposit is found upon the surface.

Diffuse gangrene sometimes originates from the circumscribed form or follows pneumonia. The diseased tissue is greenish black, mushy and soft, more or less infiltrated with fetid material. It is more serious than the circumscribed form, as septicemia may result from infectious embolism, and the case terminate fatally. When recovery takes place, the gangrenous tissue disappears by colliquation, absorption, and expectoration, leaving a cicatrix similar to those seen in hemorrhagic infarction. The healing process is greatly accelerated should communication with the bronchus facilitate the escape of the broken-down tissue.

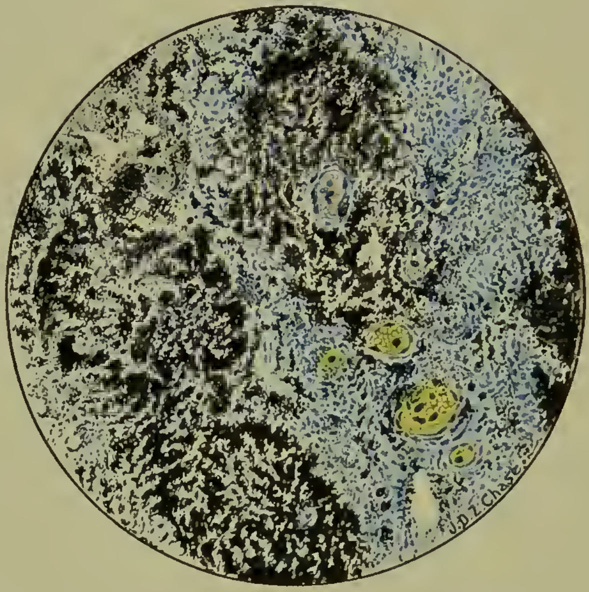

FIG. 274.—Anthracotic lung. The black areas consist of coal-dust deposited in the connective tissue of the lung, which is partly newly formed, partly preëxistent (× 100).

Pneumonokoniosis.—This is a disease of the lungs caused by the inhalation of mineral dust.

Etiology.—The disease occurs chiefly in those whose occupations cause them to frequent dusty atmospheres. Thus, coal-miners and heavers, stokers, and chimney-sweeps are apt to inhale coal-dust and soot; potters, considerable clay dust; iron filters, dust of iron and steel; glass-cutters, minute particles of glass, etc. The nature of the inhaled dusts leads to conditions which differ slightly in appearance, severity, and histologic alteration, according to the particular irritating properties which the inhaled particles possess. *Anthracosis* is caused by the inhalation of coal-dust and soot; *siderosis*, by metal dusts, such as oxid of iron, etc.; *chalicosis*, by stone-dust, pulverized quartz, glass, etc.; *kaolinosis*, by potters' clay, and *aluminosis*, by materials handled by ultramarine and porcelain workers. Small quantities of dust produce no changes of importance, and every individual living under conditions of modern civilization, where coal and wood are continually consumed in furnaces, and smoke discharged into the atmosphere, is obliged to inhale more or less dust, and consequently to exhibit some deposit in the lungs.

Morbid Anatomy.—The normal lung presents a pinkish or grayish, rather mottled, appearance, and upon the surface is divided into a large number of rounded or polyhedral lobules or divisions, outlined by lines of black that probably represent lymphatic vessels, within or around which inhaled dust has been deposited. Microscopic sections of normal lung tissue almost invariably display here and there in the interalveolar septa small, irregularly distributed black granules, usually tending to conform to the distribution of the lymphatics. These consist of inspired dusts and are of no importance. When the quantity of inhaled dust is great or its quality irritating, alveolar catarrh, with desquamation of the alveolar epithelium, transmigration of leukocytes, and hyperplasia of connective tissue may be observed. The occurrence of alveolar catarrh is invariable in pneumonokoniosis.

Much of the inhaled dust is precipitated against the walls of the upper air-passages, the nose, pharynx, and larynx, and removed through the agency of the mucous secretions, and the lashing cilia of the mucous membranes, which pass the individual particles along until they are caught in some mass of secretion about to be expectorated or discharged. The dust that reaches the air-cells is disposed of in a different way. Desquamated epithelial cells from the alveolar wall, and leukocytes are found in considerable numbers in all the air-cells, each containing a number of the dust-particles. Some of these cells escape from the air-cells, pass along the bronchial tubes, and are expectorated. The leukocytes carry their burdens into the lymphatics, where they sometimes proceed as far as the lymphatic glands, though they more often deposit them in the endothelial cells. In this way a marked accumulation of the dust occurs along the lymphatic vessels, and much larger accumulations are present in the bronchial lymphatic glands, where numbers of the leukocytes are likely to be retained. In the frequent lymph-nodes of the lung unusually large deposits of dust occur, and by irritation lead to the formation of new connective tissue.

The lung thus contains numerous fibrous nodes and nodules, generally dark in color, and varying in size from a millet-seed to a cherry. They consist of connective tissue, more or less concentrically arranged, and surrounding collections of dust-particles. When few in number, the nodes and cicatrices are chiefly at the apices and upon the surfaces of the lungs. In the smaller nodules connective tissue may be arranged about a single center, while in the nodes there are aggregations of them. When the nodules are few and scattered, the intervening pulmonary tissue, except for its pigmentation and catarrh, is practically normal. When the nodules are numerous, the intermediate substance is likely to be fibroid and dense. Cases have been seen in which whole divisions of the lung were indurated, dense, firm, atelectatic, and shrunken, so as to constitute a nodular cirrhosis.

Ziegler says that, according to its etiology and genesis, pneumonokoniosis is an inhalation bronchopneumonia, the nodules representing destroyed and indurated alveolar systems. The most marked lesions are apt to occur in the apices of the lungs. The extensive consolidations are apt to be accompanied by compensatory emphysema.

The deposition of dust in the bronchial lymphatic glands leads to a marked increase of size, the organs becoming as large as hens' eggs. The parenchyma is much softened and very dark in color, in marked cases becoming black. When the glands are incised, the softened substance escapes. This change in the quality of the parenchyma makes possible the not infrequent metastasis which occurs and which no doubt takes place, as Arnold has shown, by the erosion of small veins, and the discharge of the softened glandular substance, with its contained coal-dust, into them. Disseminated through the body in this way the dust-particles are deposited in the spleen, liver, kidneys, brain, and other organs.

Bronchopneumonia or Catarrhal Pneumonia.—Bronchopneumonia, catarrhal and lobular pneumonia are probably identical affections described by different names. It is called bronchopneumonia because it extends from the bronchioles into their ultimate distribution of infundibula and air-cells; catarrhal pneumonia, because the process is one of catarrhal inflammation, and lobular pneumonia, because the affected areas correspond to lobules of the lung.

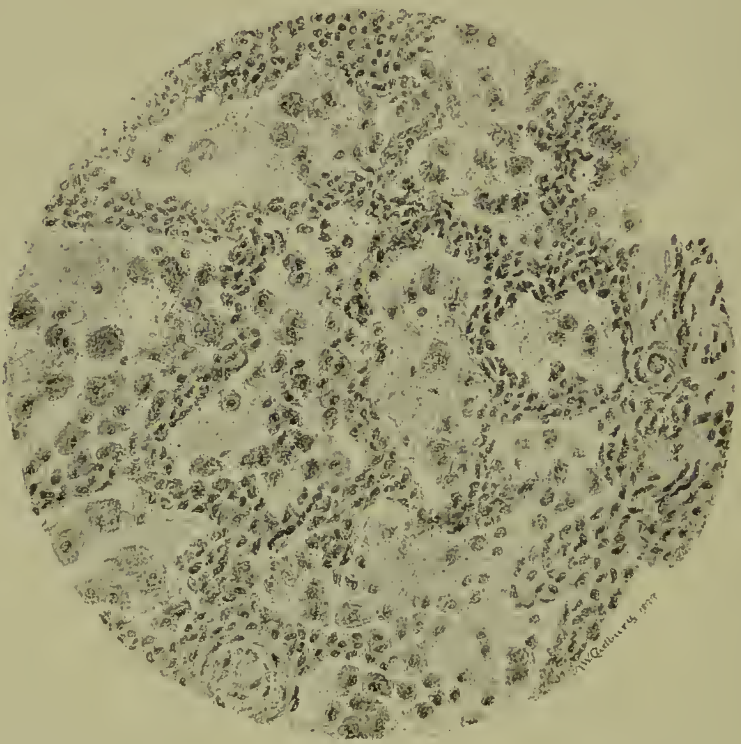

FIG. 275.—Catarrhal pneumonia, showing desquamated epithelial cells in the alveolar spaces.

Etiology.—The process is infectious in the majority of cases, depending upon the streptococcus, pneumococcus, tubercle bacillus, and sometimes upon other micro-organisms. It may also depend upon irritating dusts. Anderson divides the cases into three groups: (1) The simple acute lobular pneumonia; (2) the secondary lobular pneumonia, which usually follows infectious diseases, such as whooping-cough and measles; and (3) the embolic or suppurative, which occurs after malignant endocarditis, etc.

The causes of the disease are many. Most frequent in old age and childhood, it is occasionally seen without any assignable cause, and may be secondary to typhoid, whooping-cough, measles, scarlatina, small-pox, erypelas, emphysema, diphtheria, influenza, cirrhosis of the lungs, phthisis, tc. It sometimes succeeds bronchitis. Some cases are attributed to xposure to cold. Weak and strumous conditions and the habitual breath- ig of vitiated air seem to predispose to it. Position seems to have some redisposing influence, as among those who are long bed-ridden it is a fre- uent cause of death. The disease sometimes results from the extension of nflammation from the bronchial tubes to the air-cells.

Morbid Anatomy.—The lesions are usually irregularly distributed hroughout the lung in the form of larger or smaller conic or pyramidal atches, which correspond in shape to the distribution of a bronchiole. These areas usually project somewhat beyond the pleura. They are rather irm and hard, but are easily broken up by pinching, and when thus destroyed, allow a whitish, opaque, mucopurulent, somewhat frothy fluid to escape. The consolidated areas are usually reddish or pinkish in color, nd are often surrounded by a hyperemic zone. Two forms of the disease re described by Ziegler—the *circumscribed* and the *diffuse*. Microscopically, the disease is characterized by the presence of localized inflammatory exudations, with consolidation of lung tissue, in which the air-cells are filled by an exudate, consisting essentially of epithelial cells and leukocytes. There is usually but little fibrin in the exudation.

The naked-eye appearance of the pneumonic patch will vary somewhat according to its age and extent. Sometimes the color is dark red, sometimes grayish red, sometimes gray; the surface may be smooth, with a collection of fibrin upon the pleura, or the fibrin may roughen the surface. When incised, the areas are sometimes smooth and homogeneous, sometimes granular in appearance. The disease is of irregular duration, favorable cases usually terminating by the degeneration and disintegration of the exudate, which may be expectorated and absorbed. The condition does not affect the air-cells only, but the supplying bronchioles also invariably take part, so that one finds them hyperemic, with swollen mucous membranes, and usually occluded by an accumulation of mucus and exudate. In unfavorable cases the severity of the inflammation may bring about suppuration or gangrene of the diseased tissue, showing that very virulent bacteria have gained entrance into the tissue. In chronic cases there is no resolution or subsequent clearing up of the consolidated area, but new formation of connective tissue and a gradual transformation of the invaded area into cicatricial tissue.

Bronchopneumonia with gangrene is, fortunately, rare, and succeeds gangrene of the larynx and malignant disease of the upper air-passages.

The diffuse bronchopneumonia is scarcely correctly named. It results from the lodgment in the branches of the pulmonary arteries of infectious emboli derived from various sources. The inflammation produces nodes similar to those seen in bronchopneumonia, but much more diffuse and with a tendency to peripheral infiltration. They are apt to be coalescent and occur less regularly in pyramidal or conic areas, corresponding to bronchial distribution.

In cases of nodular catarrhal pneumonia, whether of aërogenic or hematogenic origin, if many lobules be affected and closely approximated, it is with difficulty that one can differentiate the affection from croupous pneumonia. In such cases the microscope will usually solve the problem, for it is unusual to find much fibrin in the exudates of bronchopneumonia, while in croupous pneumonia it is characteristic.

Inflammation of the smaller bronchial tubes sometimes extends directly, by contiguity of tissue, to the neighboring air-cells, irrespective of their distribution. Such cases are described as *peribronchial pneumonia*.

Bronchitis extending to the pulmonary tissues affects it differently at different times. During inspiration and expiration mucopurulent matter contained within the inflamed tubes is frequently moved outward for some distance during expiration, and then aspirated during inspiration into new, unaffected tubes, in which secondary inflammation may be started. The obstruction of the tubules caused by accumulated secretions and swelling of the mucous membrane is sometimes sufficient to cut off the air-supply and cause atelectasis. On the other hand, the air may be allowed to enter but not to escape, so that local acute distention or acute vesicular emphysema may be produced.

The **hematogenic septic metastatic pneumonia** partakes partly of a catarrhal character. It is secondary to various suppurative lesions of remote organs, and was a common surgical affection before the days of antisepsis. It is, however, occasionally seen following gunshot wounds, infected wounds, appendicitis, suppurative metritis, meningitis, hepatitis, cerebritis, etc. The pathology of the disease consists in the lodgment in the capillaries of the lung of infectious material—emboli—conveyed through the circulation. The inflammations resulting from the presence of these emboli are usually purulent. Upon inspection one finds an infarcted tissue, with a purulent center, sharply separated from the surrounding pulmonary tissue by a yellow, infiltrated zone. Ordinarily this tissue undergoes necrosis with subsequent degeneration and absorption, or may rupture into a bronchus and discharge through it. In the more serious cases gangrene may occur with the formation of a sphacelus. Upon microscopic examination of the inflamed tissue the air-cells are found filled with a hemorrhagic or cellular exudate, which frequently contains some fibrin, and thus is with difficulty separated from croupous pneumonia. The naked-eye appearance is, however, strikingly different from croupous pneumonia, and could scarcely be mistaken for it.

Severe local inflammatory processes, such as follow the lodgment of infectious emboli in the lungs, can rarely remain local affections, and from the original seat of disease the process extends to the peribronchial and interlobular vessels, which become filled with serofibrinous or purulent exudate. This lymphangitis and periangitis may also result from local pleuritis, develop over the inflamed areas, and extend along the peribronchial and interlobular lymphatics. The embolic pulmonary abscesses sometimes rupture through the pleura, and lead to empyema, or, if prior agglutinative inflammation has fastened the parietal and visceral pleuræ together, to rupture through the diaphragm into the abdominal cavity, or even externally through the chest-wall. The septic pneumonia is apt to be a fatal affection, and forms one of the most serious complications of surgery.

Croupous or **fibrinous pneumonia** is one of the most frequent and most serious of the pulmonary affections.

Etiology.—It is an infectious, inflammatory disease of the lung, caused by the pneumococcus of Fränkel and Weichselbaum. Presenting all the appearances of a local inflammation of the lung, it is in reality an infection of manifold occurrence, which most frequently begins in the lung. Similar affections at times depend upon other micro-organisms, such as the streptococcus, the staphylococcus, the bacillus of Friedländer, and perhaps even at times the typhoid bacillus, so that fibrinous pneumonia is not always a clear-cut definite process. It is usually a primary affection, but sometimes occurs as a sequel of other infectious diseases, such as typhoid, rheumatism, influenza, measles, etc., and sometimes in non-infectious diseases, such as nephritis. It is in these latter cases that the occurrence of the streptococcus, the staphylococcus, the typhoid bacillus, etc., is apt to occur, while the pneumococcus is almost invariably associated with the primary cases.

Bacteriology.—The *pneumococcus* of Fränkel and Weichselbaum, called by Sternberg the *Micrococcus pneumoniæ crouposæ*, and by Telamon the *Diplococcus lanceolatus*, is the micro-organism most constantly present in croupous or fibrinous pneumonia. It is commonly spoken of as specific, though conditions closely resembling croupous pneumonia are sometimes caused by other organisms.

The coccus was first observed in his saliva by Sternberg in 1880, and described as *Micro-occus Pasteuri.* The following year Pasteur also observed it in saliva. Fränkel, who further nvestigated it, called it the *micrococcus of sputum septicemia.* Weichselbaum showed its etiologic relationship to croupous pneumonia, and called it the *Diplococcus pneumoniæ.* Subsequent workers confirmed the work of these pioneers, and as it is agreed that the organism is coccus, and that it is etiologically concerned in pneumonia, it has come to be called the *pneumococcus.*

Morphology.—The pneumococcus varies somewhat in morphology, according to the conditions under which it develops. In the blood of men or animals infected, and in the "rusty sputum" of pneumonia, the organism appears for the most part in pairs, each pair consisting of two somewhat lancet-shaped or elongated cocci. Each is surrounded by a distinct halo or capsule. The cocci are quite small, measuring not more than 1 μ in the longest diameter. When grown in artificial culture upon agar-agar, they appear more nearly spheric, seldom appear in distinctly diplococcal arrangement, and show no capsules. In liquid cultures they occasionally show a narrow capsule, are nearly spheric, and may form long chains as well as diplococci. There are no spores. The coccus is not motile and has no flagella.

Distribution.—Of the distribution of the pneumococcus in nature we know very little. It seems to be a frequent inhabitant of the respiratory apparatus, though it is not certain that it is a harmless one. The statement formerly made that it constantly occurs in normal saliva is not borne out by experiment. It is found in a variety of inflammatory processes, both primary and secondary, among which may be mentioned pneumonia, meningitis, emphysema, otitis, endocarditis, and liver abscess. It also occurs in many secondary complications of pneumonia and other primary affections.

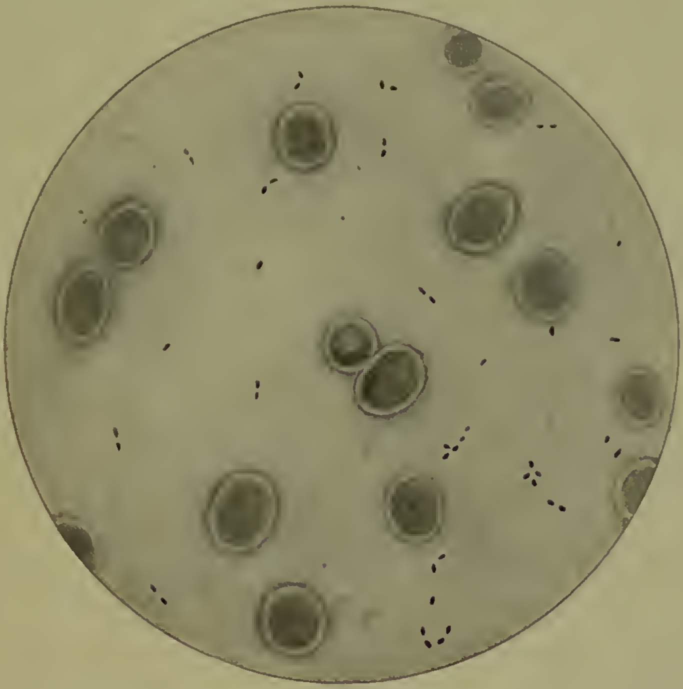

FIG. 276.—Capsulated pneumococci in blood from the heart of a rabbit; carbol-fuchsin, partly decolorized (× 1000).

After an attack of pneumonia it becomes a regular resident of the respiratory apparatus of the convalescent, and has been found virulent in the saliva *nine years* after convalescence from the disease.

Staining.—The organism stains well with the usual anilin-dye solutions and very well by Gram's method. The capsules usually show quite well, though special methods have been recommended for staining them.

Cultivation.—The artificial cultivation of the pneumococcus is not difficult, as it grows quite readily for a few generations in ordinary media. The most ready method of isolation is to infect a rabbit or a mouse with the rusty sputum of a pneumonic patient, wait until the animal dies, open the body under strict aseptic precautions, and cultivate the coccus from the heart's blood. It grows in bouillon with the production of a slight cloudiness and an acid reaction.

Upon the surface of coagulated blood-serum, agar-agar, glycerin agar-agar, and obliquely solidified gelatin it grows with the production of minute, round, homogeneous, dew-drop-like colonies, which rarely become confluent. When the colonies are examined under a lens, it is found that they are granular, and when examined superficially, spread from a central nucleus. The gelatin is not liquefied, and no visible change is produced in any of the media by the growth of the organism. Milk is coagulated by the pneumococcus. It is an optional anaërobe.

The organism grows between 24° C. and 42° C., but most rapidly at 37° to 38° C. It never grows luxuriantly, and unless frequently transplanted to new media, rapidly dies out. Frequently transplanted cultures soon lose their virulence, and I think the best method of maintaining the virulence of the organism is by constant transplantation from rabbit to rabbit.

Pathogenesis.—The pneumococcus is pathogenic for mice, guinea-pigs, and rabbits. Dogs are said to be nearly immune. The varying virulence of the organism and the differing susceptibility of the animal infected determine the character of the infection. In some cases the pneumococcus makes its appearance in abscesses of the middle ear and other deeply seated parts, and may remain as a local infection, or may spread to the meninges and cause fatal meningitis. Some cases of cerebrospinal meningitis seem to depend upon pneumococcus infection. In other cases infection beginning in the lungs causes croupous pneumonia, which remains a local pulmonary infection or may become a septicemia by the entrance of the bacteria into the circulation. The outcome of experimental infections in susceptible animals will depend upon the mode of introduction, though ultimately all infections become fatal septicemias. Thus, when introduced through the chest-wall into the lung, a pneumonia similar to croupous pneumonia of human beings occurs. When introduced into the peritoneum or other serous cavity, a fibrinous inflammation of the membrane occurs. If the infection be subcutaneous, at the seat of inoculation an extensive fibrinohemorrhagic exudation occurs. In all these cases, however, death finally occurs from septicemia.

In cases of human infection, in which pneumococcus septicemia follows, croupous pneumonia, endocarditis, meningitis, and other remote lesions may occur, or death may result immediately from the septicemia.

The fibrinous character of the pneumococcus exudations seems to indicate that the organism produces a strong fibrin ferment, but this cannot be proved by experiment.

Immunity.—A very brief or imperfect immunity succeeds pneumococcus infection. The immunization of animals to this organism is difficult. Pane, De Renzi, Washbourne, McFarland, Lincoln, and others have achieved it, but whether or not the serum of these animals is of therapeutic value is questionable.

The investigations of Netter havè shown the pneumococcus to occur in man in the following relative frequency in primary infections:

1. ADULTS:

Pneumonia	65.95 per cent.
Bronchopneumonia	15.85 "
Capillary bronchitis	15.85 "
Meningitis	13.00 "
Emphysema	8.53 "
Otitis	2.44 "
Endocarditis	1.22 "
Liver abscess	1.22 "

2. CHILDREN—of 46 cases investigated:

Otitis media	29 times.
Bronchopneumonia	12 "
Meningitis	2 "
Pneumonia	1 time.
Pleurisy	1 "
Pericarditis	1 "

Friedländer's Bacillus; Friedländer's Pneumococcus; Bacillus mucosus capsulatus; Bacillus pneumoniæ.—This organism was discovered in 1883 by Friedländer, in the exudate from a pneumonic lung, and was supposed by him to be the specific cause of pneumonia.

Morphology.—The organism is distinctly bacillary in its morphology, though some individuals are so short as to suggest cocci. It has rounded ends, and is surrounded by a distinct halo or capsule. There are no spores and no flagella, and the organism is not motile.

Staining.—The organism stains well by ordinary methods, but not by Gram's method.

Distribution.—Friedländer's bacillus is a common inhabitant of the respiratory apparatus, where it seems to be a harmless saprophyte under conditions of good health. In diseases of the respiratory organs it seems to grow rapidly and contribute to the disease process, and sometimes acquires disease-producing powers of it own. It is commonly found together with the pneumococcus in croupous pneumonia, and sometimes seems to be the predominating organism, especially in catarrhal pneumonias. Smith has seen some cases in which the alveolar spaces were filled with masses of the bacilli.

These bacilli have also been found in the throat, both in simple inflammations and in diphtheria. Howard has obtained them from the antrum of Highmore and frontal sinuses in suppurative inflammation of these parts, and from perirenal abscess, peritonitis, and endometritis, so that they seem to be wide-spread in distribution and of considerable importance.

Cultivation.—The bacillus is easily obtained by the plate method of cultivation, as it is luxuriant in its growth upon artificial media. At the end of twenty-four hours, upon gelatin plates, small white spheres make their appearance and tend to spread upon the gelatin so as to form white masses of considerable size. When examined with a lens, the colonies appear irregular in outline and somewhat granular.

In gelatin puncture cultures the organism shows its ability to grow both with and without oxygen. Upon the surface in the presence of oxygen it grows best, forming a flattened, spreading mass. In the puncture it forms a series of small, confluent, spheric colonies. The growth resembles a nail. The gelatin is neither liquefied nor softened. Upon agar-agar, glycerin agar-agar, and blood-serum the organism forms a luxuriant growth, white or brownish-yellow, and smeary in appearance. An abundant growth takes place upon potato, quickly covering the surface with a thick, yellowish-white layer which sometimes contains bubbles of gas.

In all culture-media containing sugar an abundant formation of gas-bubbles occurs.

Pathogenesis.—Experimental inoculation with Friedländer's bacillus commonly fails to produce any pathogenic effects. Friedländer himself reports that the organism is feebly pathogenic for mice and guinea-pigs.

Morbid Anatomy.—The disease is characterized by the occurrence of a large amount of an exudate whose chief characteristic is rapid coagulation with the formation of considerable fibrin. It affects one or several lobes, a whole lung, or rarely both lungs. Double pneumonia is usually fatal, as the amount of breathing-space is too small to permit of proper aëration of the blood. The affected lung tissue is swollen, so that the lung is larger than normal, and is firmly consolidated and liver-like in texture, the air being entirely displaced by the coagulated exudate in the cells. A fragment cut from a lung immediately sinks if placed in water. The color of the consolidated tissue varies according to the duration, or perhaps according to the rapidity of the disease process. Sometimes the lung is dark red, sometimes pinkish gray, sometimes gray in color. The pleura is usually smooth, except for adherent flakes of fibrin. In the pleural cavity one is apt to find a fluid exudate with floating flakes of fibrin. When incised, the lung tissue appears granular, and if it be scraped with a knife, little fibrinous plugs are drawn out of the air-cells and bronchioles. The amount of fluid contained in the tissue varies: when the color is red, there is usually more fluid than when it is gray, and the darker the color of the tissue, the richer it is in fluid. The texture of the lung tissue seems to be altered, for, whereas ordi-

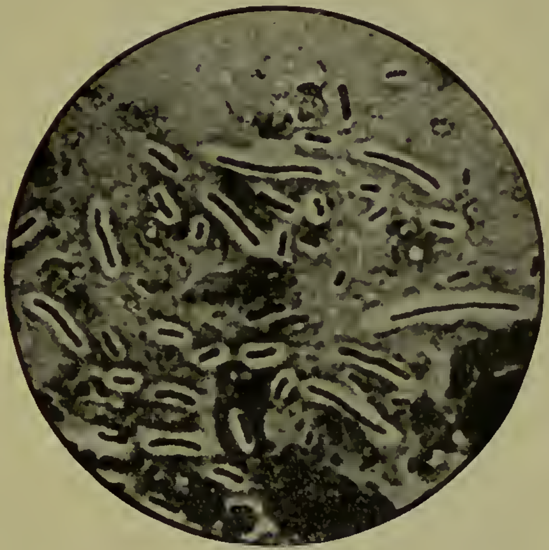

FIG. 277.—Bacillus pneumoniæ of Friedländer, from the expectoration of a pneumonia patient (× 1000) (Fränkel and Pfeiffer).

narily one finds the spongy character of the lung tissue preventing its ready laceration, the pneumonic lung appears much more readily torn than normal.

The consolidated tissue resembles so closely liver tissue that it has become customary for the diseased tissue to be described as *hepatized.*

It was at one time supposed that this disease ran a regular course of three definite stages: First, a stage of *congestion;* second, one of *red hepatization;* third, one of *gray hepatization*, and then finally underwent *resolution* and recovery if the patient lived. The fact that one often observes cases in which gray hepatization occurs without preceding red hepatization. and that red hepatization has been found where gray was expected, makes us skeptical as to the correctness of this mode of description though it affords opportunity difficult to secure in any other way.

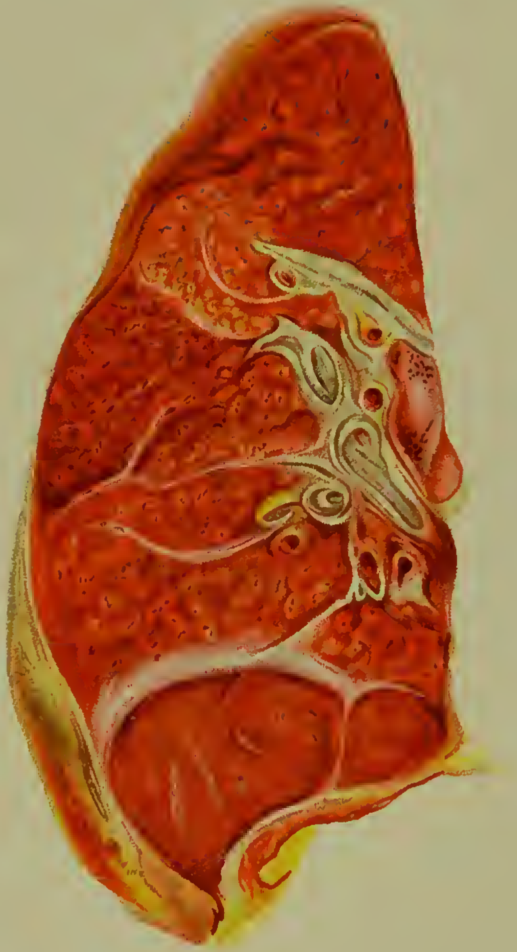

FIG. 278.—Lung of a child, showing the appearance of the organ in the stage of red hepatization of croupous pneumonia. The pneumonia has been preceded by chronic pleuritis, which accounts for the thickened fibrous trabeculæ extending into the tissue, and which may have had something to do with the peculiarly prominent appearance of the bronchioles throughout the lung (from a specimen loaned the writer by Dr. Joseph Sailer).

Stage of Congestion.—This is a preliminary active hyperemia. The pulmonary vessels are full of blood, the lung abnormally red in color and abnormally voluminous. The tissue, when pressed upon, readily pits, showing that there are a loss of elasticity and some edema. Crepitation is lessened. The lung is heavy. When incised, a sticky red fluid, usually containing air-bubbles, escapes from the tissue. It is scarcely possible to differentiate between the prepneumonic congestion and congestion from other causes. When examined microscopically, the lung shows marked turgescence of the capillary vessels, with the escape into the air-cells of a considerable amount of fluid, rich in red blood corpuscles. This exudate may also contain a few leukocytes, and usually shows quite a number of desquamated epithelial cells. The crepitant râles which characterize the congestive stage of pneumonia are caused either by the bubbling of air through the viscid fluid, or by the sudden separation of the adhering alveolar walls.

Red Hepatization.—Supposing that the disease progresses from congestion to red hepatization, we conceive that the escape of exudate into the air-cells is followed by its coagulation and the complete exclusion of air. The lung remains dark red in color, entirely ceases to crepitate, is solid, cuts exactly like liver, and is friable.

When examined microscopically, the air-cells and small bronchial tubes are all found filled by the coagulated exudate. At first glance the air-cells appear to be filled with red blood-corpuscles, but upon more careful examination the delicate reticulum of fibrin, the more delicate filaments of which extend among the red blood corpuscles, becomes apparent. There may be no leukocytes, or a good many may be observed in the air-cells. The desquamated epithelial cells are inconspicuous. It is a characteristic that the air-cells shall be full of the exudate, which seems to cling to their walls and leave no room for the entrance of air. The blood capillaries are congested.

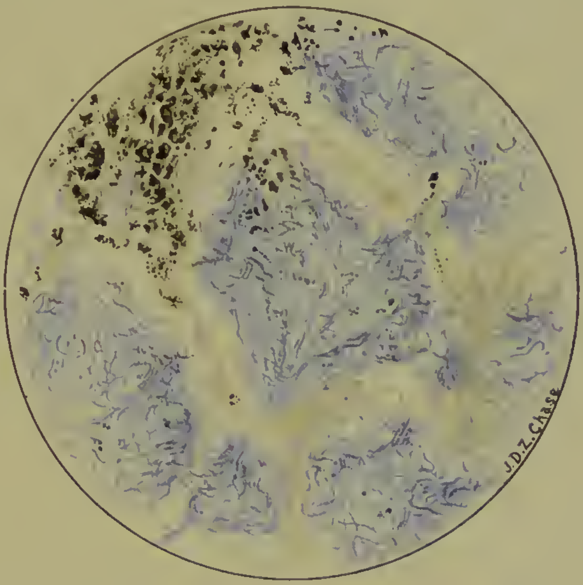

FIG. 279.—Croupous or fibrinous pneumonia, stage of red hepatization; stained by Weigert's method to show the fibrin only. The blue threads filling the air-cells consist of fibrin-filaments (× 180).

Gray Hepatization.—Gray hepatization is supposed to mark the beginning of recovery. It is called gray, from the naked-eye appearance. The tissue of the diseased lung having changed its color from red to gray without any important alteration in texture, the microscope alone is able to explain how the change takes place.

When examined microscopically, one finds that the red blood corpuscles so conspicuous in the preceding stage have undergone various degenerative changes and been resolved into molecular débris. The fibrin has also in large part disappeared, probably through colliquation, and the air-cells are seen to contain large numbers of leukocytes. Their presence is supposed to depend upon the chemotactic powers of the bacteria and tissue remnants, and their object is that of scavenging and cleaning up the lung. It is in the stage of gray hepatization that one notes a separation of the clinging exudate from the walls of the air-cells and the beginning of the entrance of air into the lungs, so that more and more air enters as the contraction of the organ and removal of the exudate make room for it.

Resolution.—This stage, which varies in duration, marks the final return of the pulmonary tissue to the normal. The softened exudate is partly absorbed and partly expectorated; the leukocytes completely remove the remaining molecular matter and the lung returns nearly to its normal condition.

The lesions are always homogeneous, and do not spread from any single focus that can be pointed out. It sometimes happens that neighboring lobes present different stages or different ages of the disease, but in each of them that process present will be homogeneous throughout. The unaffected portions of pneumonic lungs present other less important changes. There is often compensatory inflation, and the tissue is usually pale, though not infrequently congested. One finds enlargement and inflammation of the bronchial glands, which appear reddish or brownish in color. It must not be forgotten that the disease is both infectious and toxic. Septicemia, from the entrance of the pneumococci into the circulation, is very common and explains the frequency with which endocarditis, pericarditis, meningitis, and other secondary processes occur in the course of pneumonia. The toxemia explains the chill, fever, circulatory and other severe symptoms not sufficiently explained by the respiratory obstruction.

The disease usually runs a short course, terminating by crisis, immediately succeeded by the beginning of resolution. Occasionally the severity of the inflammation is so marked, or the liability to other infections so increased, that abscess formation and gangrene of the lung occur. These seem, however, to be accidental and, fortunately, uncommon sequelæ of the disease.

Caseation has been pointed out as a termination of croupous pneumonia, but experience seems to indicate that caseation does not occur in a lung not previously tuberculous. It is true, however, that the occurrence of pneumonia in a tuberculous lung facilitates the development of the original disease. It is held by some that the hyperemia attending croupous pneumonia has the tendency to hold tuberculous processes in abeyance or to check them, so that after pneumonia a tuberculous disease advances less rapidly than before. Such cases are probably extremely unusual. Indeed, most clinicians hold the contrary opinion—that the changes resulting from croupous pneumonia predispose to tuberculosis rather than antagonize it.

An unfortunate, not very frequent, termination of pneumonia is **postpneumonic induration.** The tissue becomes carnified, and continues to have somewhat the appearance of the stage of red hepatization, but is not so dense and not granular on the cut surface. When examined microscopically, the tissue is found to be very cellular, due to an active proliferation of the interalveolar cellular tissue and a wide-spread cellular infiltration. This is followed by marked hyperplasia of connective tissue, by which the septa are thickened. Ziegler calls attention to the fact that within the air-cells one occasionally finds a fibrinous plug replaced by new fibroconnective tissue. The connective tissue is not all in the interalveolar wall, but grows into the air-cells as nodular masses. The bronchial, peribronchial, and interlobular tissues increase in amount, the lung becoming indurated and fibrous, and subsequently contracting so as partially to close or much diminish the size of the air-cells.

Should the alveolar epithelium be lost, the air-cells may be entirely obliterated by the union of their approximated walls.

The fibrosis is not uniform, but is distributed beneath the pleura, around the bronchi, and in the neighborhood of interlobular connective tissues. No circumscribed nodes are formed, the lesions always occurring in bands or layers which gradually blend with the healthy lung tissue. The pleura may become involved, with resulting hyperplasia of its connective tissue as well as of the subpleural connective tissue connecting with the interlobular bands, thus bringing about alterations in the bronchial vessels, lymphatics, and in the contiguous pulmonary tissue. The affected lung may thus be deformed by subsequent contraction and appear abnormally small, rounded, encapsulated, and indurated from the irregularly distributed, solid, and normal tissue. Intervening emphysema and occasional bronchiectasis may also be present.

Pleura in Pneumonia.—The pleura covering the pneumonic lung is invariably more or less inflamed and coated with fibrin. The surface of the swollen lung is somewhat indented by the ribs. Sometimes in gray hepatization, especially in elderly people, the contrast between the grayish contents of the pulmonary alveoli and the black pigmented interalveolar tissue gives the lung a peculiar marbled appearance.

Pleurogenic pneumonia has its origin in the inflammation of the pleura. As in inflammations of the lung the pleura is inflamed, so in inflammations of the pleura the subjacent pulmonary tissue is inflamed, and presents a picture identical with that seen in some of the pneumonic conditions already described. The inflammatory process is not limited to an extension by continuity of tissue, which, of course, takes place, but extends to the deeper and more remote parts of the pulmonary tissue by way of the interlobular and peribronchial lymphatic vessels. The more severe the infectious process in the pleura, the more wide-spread the secondary invasion will be, so that in empyema pulmonary abscesses may occur. Pleurogenic pneumonia is probably more common in children than in adults. In marked cases the pathologic alterations are of interest. Lines of suppuration may occur as yellow-white stripes separating the lobules of the lung from one another. Other purulent extensions along the course of the bronchi appear in transverse section as yellowish, circumscribed zones about the bronchi. There may be purulent secretion within the tubes as well. By causing suppuration in the interlobular tissue of the lung, pleurogenic pneumonia may cause an actual dissection of the lobules from one another, this being known as **dissecting pneumonia.** The tissue between the distended lymphatic vessels is usually dark red from hyperemia; it may be empty of air, and the air-cells filled by an exudate similar to that seen in catarrhal pneumonia. The subpleural pulmonary tissue is infiltrated with round-cells, the pleura appearing very much thickened from cellular infiltration and inflammatory exudation, and not infrequently there is some fibrin in the exudate which enters the air-cells, approximating the surface of the lung.

Not only do inflammations of the pleura lead to inflammations of the pulmonary tissue, but inflammations of other neighboring organs not infrequently lead to a secondary invasion of the lung, so that in mediastinal abscess, bronchial lymphadenitis, and various diseases of the esophagus, vertebræ, and even abdominal organs, such as the stomach and liver, inflammations of the lung may occur.

Tuberculosis of the Lungs.—Tuberculosis of the lungs—phthisis pulmonalis, pulmonary consumption, etc.—is one of the most frequent pulmonary diseases.

Etiology.—The disease is caused by the tubercle bacillus; the typical lesion is the miliary tubercle. The bacilli may enter the lung through any one of three different channels: First, and probably the most frequent, through the respired air; second, by the blood from the intestine; third, through the lymphatics from neighboring tuberculous foci. Ultimately all three processes run similar courses, and can with difficulty be disassociated.

Aërogenic Pulmonary Tuberculosis.—Starting with the most frequent form of infection, in which the cause of the disease is carried into the organ with the inspired air, we find that the micro-organism obtains a nidus either in the air-cells or in the smaller bronchioles. The apex of the lung is most frequently the point of primary infection. The first change brought about in the air-cell in all probability partakes of the nature of a mild catarrhal inflammation. The epithelial cells are desquamated, leukocytes transmigrate, and the infected air-cell becomes filled up by a cellular accumulation that

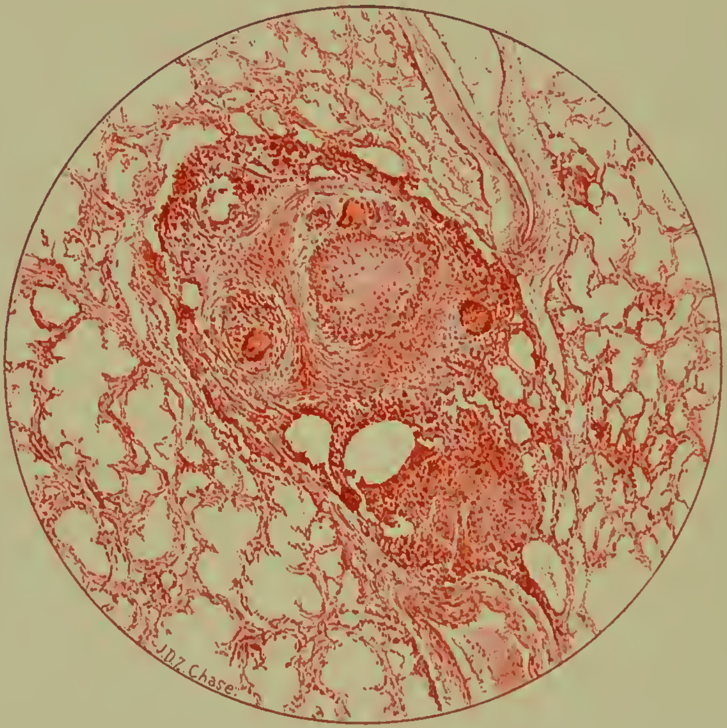

FIG. 280.—A miliary tubercle of the lung, consisting of two, probably three, submiliary tubercles. The coagulation-necrosis of the center and the giant-cell formation are well shown (× 70).

forms the primitive tubercle. The bacilli may grow in the air-cells, or almost immediately after their entrance into them may be picked up by leukocytes and carried into the lymphatic channels, so that the primitive tubercles may be either interstitial or alveolar. With the increase in number of the tubercle bacilli occurs a simultaneous increase in the size of the tubercle, which soon encroaches upon neighboring air-cells, so that its catarrhal inflammatory effects, transmitted through the alveolar wall, cause the neighboring air-cells to inflame and become filled with an inflammatory collection similar to that seen at the original focus. The formation of large lesions depends upon continual invasion of fresh air-cells and infiltration of intervening septa. In this way the tubercle remains a circumscribed, solid, inflammatory node of varying size, composed of a group of air-cells destroyed by a solid accumulation within them and by a cellular infiltration of their walls. The air-cells immediately about this tubercle are always found to exhibit more or less catarrhal inflammation.

The increase in the size of the original lesion might go on indefinitely if certain accidental factors did not coöperate against it. Thus we find with the infiltration of the interalveolar septa destruction and obstruction of the capillaries. In the tuberculous tissue no new capillary blood vessels are formed, so that there soon comes a time when the nutrition of the inflammatory tissue is outgrown, and coagulation necrosis sets in and both cells and micro-organisms at the center of the tubercle die, the younger tubercle bacilli being found in large numbers only in the newly invaded tissue. The tubercle bacilli are in all probability frequently picked up by leukocytes or other phagocytic cells, and carried to the lymphatics, where they seem to overpower their captors, grow, and produce secondary tubercles. It may also be true that the lymph-currents themselves occasionally detach and carry away the tubercle bacilli, and remembering the great blood vascularity and equally great lymph vascularity of the pulmonary tissues, it is easy to understand how a focus of tuberculous disease may become a center from which the process extends in all directions, and leads to an extensive invasion of the lung.

While this is going on the size of the original lesion continues to increase by the incorporation of outlying tubercles as they are reached. The center is continually degenerating—that is, caseating. Cavities are formed of tuberculous tissue in various ways: for example, from a large, caseous, primary lesion, or from a similar secondary lesion, the extension of the tuberculous disease into the bronchial tube may offer an opportunity for the escape of the softened, necrotic center of the tuberculous mass. In this way a ragged hole is formed, small in the beginning but continually tending to increase in size. Such a cavity presents an irregular wall of yellowish or yellowish-gray, cheesy, tuberculous tissue. The bronchial vessel from which its contents escape may appear to enter at one side and leave it at the other, or may enter and apparently not leave it, the proximal portion having been obliterated by the tuberculous inflammation or plugged by inhaled secretions. If thick-walled blood vessels occur in the immediate surroundings, they may appear as ridges upon the walls of the cavity, or may extend as cords directly through it. The distending influence of the inspired air will always aid in increasing the size of cavities. The entering air brings into the cavity mucous secretion from the inflamed bronchioles with which it connects, and with this secretion, bacteria of putrefaction or of suppuration, which, by developing in the necrotic material within the cavity, cause a rapid destruction of the tissue and somewhat change the natural order of events, by the production of purulent or even gangrenous lesions. At other times the wall of a bronchial vessel is weakened, without being perforated or eroded by the tuberculous process, when bronchiectasis occurs.

The erosion of blood vessels within tuberculous cavities not infrequently causes hemorrhage. If capillaries are eroded, the hemorrhage is slight and the sputum blood-stained. If large vessels rupture, the hemorrhage may be large or even fatal. Blood vessels with tuberculous, weakened walls dilate, with the formation of small aneurysms, which, should they rupture, produce severe and sometimes fatal hemorrhage. The presence of escaped blood into the tuberculous cavity facilitates the growth of saprophytic bacteria, and thus aids the further progress of the secondary infections. The pulmonary tuberculosis is invariably associated with bronchitis, the mucopurulent discharges from the inflamed tubes, mixed with the necrotic material from the cavities, forming the sputum so characteristic of the affection.

During the time that the cheesy material is being discharged from the cavity into the tube with which it communicates, and while the tuberculous area is disseminating its infectious micro-organisms through the lymphatics and thus invading new tissue, there is a continual backward and forward movement of infectious material in the air-passages of the lung, constantly invading new parts of the bronchial tree. With each expiratory effort the infectious matter is carried outward; with each succeeding inspiratory effort it is carried back again into deeper and heretofore uninvaded air-passages, so that a triple infection is continually in progress: (1) By continuity of tissue; (2) through the lymphatics; (3) through the air-tubes. Thus, from a single primitive lesion of the lung, the whole organ may become involved and transformed into an almost unrecognizable, consolidated, cheesy, eroded, and cavernous mass of diseased tissue.

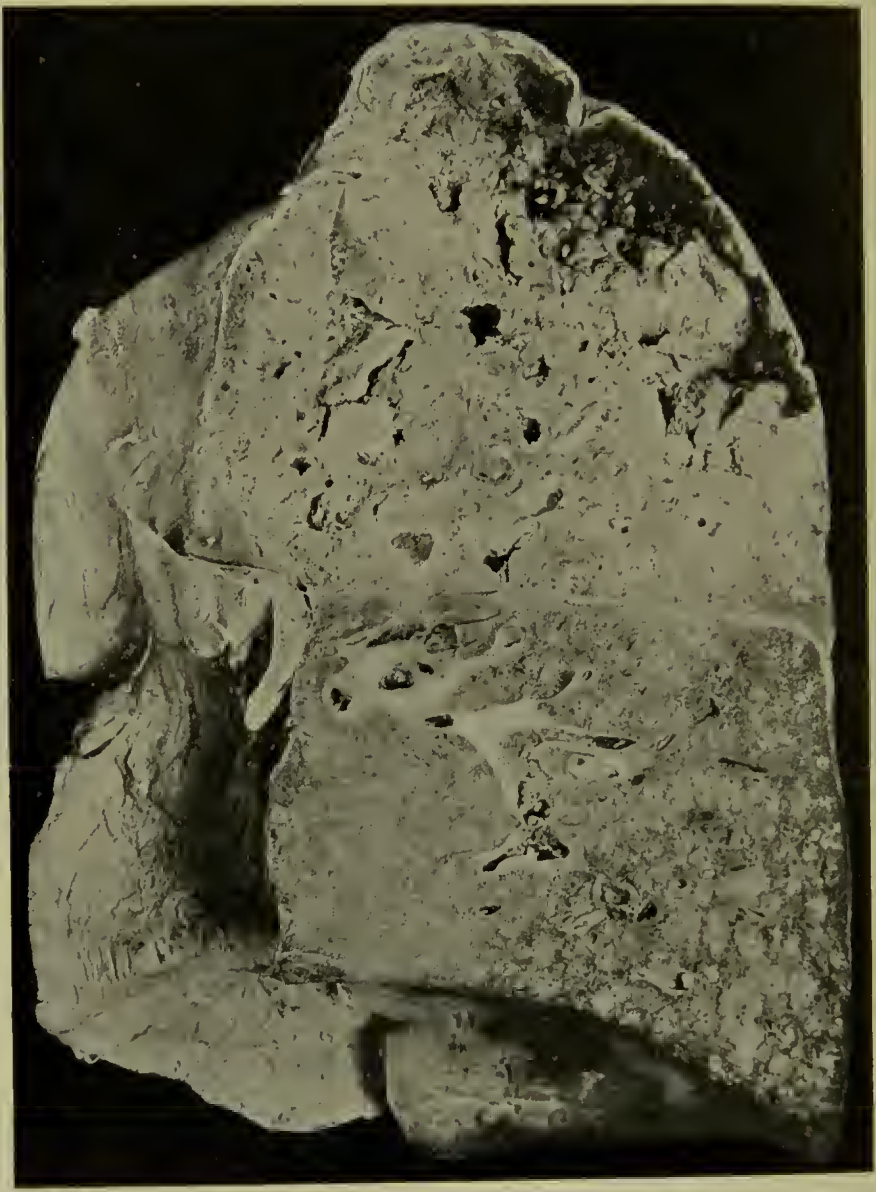

FIG. 281.—Tuberculosis of the lung: the upper lobe shows advanced cheesy consolidation with cavity-formation, bronchiectasis, and fibroid changes; the lower lobe retains its spongy texture, but contains numerous miliary tubercles.

The disease of the lung usually does not progress very far before tuberculous changes are inaugurated within the bronchial lymphatic glands. It is interesting that the disease of these organs is subordinate to that of the lungs, and only in rare cases progresses more rapidly than the original lesion. Occasionally the erosion of a blood vessel enables infectious material to enter the blood-stream, and, by disseminating the bacilli through the systemic circulation, occasions *general miliary tuberculosis*.

Hematogenous Pulmonary Tuberculosis.—In this form of tuberculosis the primary lesion, instead of occurring within air-cells, takes place within capillary blood vessels. The bacilli are not inspired, but carried to the lung from tuberculous foci elsewhere, in the form of minute emboli. They probably enter the thoracic duct by way of the lacteals with the products of digestion, reach the venous circulation, and are then conveyed to the lungs. Should a single embolus containing a tubercle bacillus thus enter the lung, a miliary tubercle will be formed, differing from other miliary tubercles only in that its primitive cells have been derived from the endothelium of the capillary blood vessels and from the cells of the surrounding interalveolar tissue. Before the tubercle attains visible dimensions it encroaches upon the air-cells and occasions within them a catarrhal inflammation identical with that already described in connection with the aërogenic tubercles. One by one the neighboring cells are filled up and included, and thus in a short time a lesion similar to that already described will be formed.

It often happens that great numbers of tubercle bacilli are carried to the lung by the venous blood from tuberculous lesions of the spinal column, testicle, joints, etc., in a short time causing the formation of a great number of miliary tubercles. Sometimes both lungs appear filled with equally distributed, minute tubercles, originating in this manner. This is called *miliary tuberculosis of the lung*.

Lymphogenic Pulmonary Tuberculosis.—The lymphatic form of pulmonary tuberculosis most frequently succeeds tuberculosis of the bronchial glands and pleura, the tubercle bacilli being carried from these tissues into the lung tissue itself *via* the lymphatics. In tuberculous bronchial lymphadenitis the perforation of the enlarged, softened, and ulcerating glands into a bronchus or even into the lung itself, followed by discharge of their contents into the air-passages, causes what is really a form of secondary aërogenic tuberculosis.

Tuberculous extension takes place from the pleura both by continuity of tissue and by distribution of the bacilli along the lymphatic vessels of the pulmonary septa and those about the bronchial vessels. There is usually little difficulty in detecting the pleurogenic pulmonary tuberculosis, as the diseased pleura is so altered in appearance as to be quite characteristic.

The tubercle formation or *eruption* is accompanied by more or less hyperemia of the surrounding lung and by alveolar and bronchial catarrh. The bronchi usually manifest signs of inflammation; the mucous membrane is red, may contain a mucopurulent, sometimes a bloody, material. When many tubercles are present, the lung is consolidated and denser and contains less air than normal. The exclusion of air from the lung is always in proportion to the amount of consolidated pulmonary tissue. When the tuberculous areas are of large size, the tissue appears solid, yellowish or grayish, sometimes friable, sometimes softened, and creamy or even purulent. Cavities when present appear as irregular spaces in the consolidated tissue. Sometimes neighboring cavities communicate with one another.

The tuberculous disease may be confined entirely to one lung, but it is somewhat unusual to find advanced tuberculosis of one lung without some involvement of the other. The lungs are rarely uniformly affected, the disease usually being much more advanced in one than the other. The disease is rarely limited to the natural divisions of the lung, several or all of the lobes of the diseased lung being simultaneously, though not equally, affected.

In advanced cases the disease may transform an entire lung into a consolidated mass of yellowish tissue, riddled with cavities, divided up by dense bands of connective tissue, and covered with a thickened pleura, and devoid of any resemblance to normal pulmonary tissue.

The remaining air-containing portions of the lung are rarely normal in appearance, because of an acute or chronic distention (compensatory emphysema). Along the free borders of the lung, and here and there upon its surface, one finds groups of distended air-cells. The plugging of the bronchial vessels with secretions and cheesy matter from the cavities, and the obliteration of the smaller bronchial tubes by the development of tubercles in and around them and the swelling of their lining membrane, predispose to atelectasis. Fresh atelectasis in the tuberculous lung is common.

Bronchopneumonia is a common secondary process in tuberculosis of the lungs, depending upon the entrance of infectious material. It is usually, but not always, tuberculous in nature, and tends to diminish the air-space by increasing the amount of consolidated tissue.

Tuberculous Pleuritis.—Tuberculosis of the lung rarely progresses to any considerable extent without affecting the *pleura*, which is at first likely to undergo a simple local inflammation over the tuberculous area, but very frequently becomes agglutinative, so that the parietal and visceral pleuræ unite. When this does not occur, the pleura over the tuberculous lung almost invariably becomes much thickened, and not infrequently exhibits a number of miliary tubercles upon its surface, or immediately beneath it. In the more chronic cases the thickening of the pleura probably aids the progress of the disease by keeping the lung from properly expanding.

According to the course of the disease different appearances are presented. Thus, when the progress is extremely rapid, the lung may consolidate so quickly and uniformly as to bear a close resemblance to the stage of gray hepatization of croupous pneumonia. In such lungs there may be no excavations or cavities. This is sometimes spoken of as *tuberculous pneumonia*. When less rapid and accompanied by consolidation with numerous small excavations, the condition which leads to a rapid fatal termination is spoken of as *phthisis florida*. The ordinary form, which is familiar to every practitioner and soon becomes familiar to every student, is that in which the disease is of months' and sometimes of several years' duration. It is usually called *caseofibroid phthisis*, and seems to indicate some resisting power on the part of the patient.

In the caseofibroid tuberculosis of the lungs, together with cheesy areas, excavations, fresh miliary tubercles, bronchiectasis, emphysema, atelectasis, etc., one finds also new formation of connective tissue, sometimes surrounding tuberculous areas, sometimes taking on the form of a hyperplasia of the pulmonary trabecula and peribronchial tissue, which seems to indicate a tendency of nature to shut off, encapsulate, or organize the specific inflammatory lesions. Extensive areas of tissue may show marked connective-tissue formation, but though healing is in progress in some parts of the organ, the destructive lesions are steadily gaining upon it elsewhere, and ultimately the individual is obliged to succumb.

Rarely the disease takes an essentially chronic course in which the multiplication and dissemination of tubercles are held in abeyance for years by an enormous hyperplasia of connective tissue, surrounding, encapsulating, and isolating the tuberculous areas. Unfortunately, however, in *fibroid phthisis* the connective-tissue formation is itself far from benign, and the isolating and encapsulating bands, when they subsequently contract, deform the lung, diminish its size, distort the chest (especially when pleuritic adhesions exist), and diminish the breathing space.

Recovery from Pulmonary Tuberculosis.—Recovery occurs when the immunity of the patient checks the further spread of the disease. It takes place by organization, encapsulation, isolation, and subsequent calcification of the lesions already present. It is quite probable that it is not less the encapsulating barrier formed to limit the disease than that peculiar resisting power of the individual which enables the barrier to be formed that predisposes to recovery. The isolated and encapsulated tuberculous tissue undergoes caseation, and in it both cells and tubercle bacilli seem to die. In the molecular débris lime-salts are usually deposited. It is quite common to find firm fibroid and calcified tuberculous nodules in the apices and sometimes in the lower lobes of the lungs of individuals dying from other affections. In size they vary from that of a pin-head to that of a pigeon's egg. They are firmly encapsulated in the connective tissue, and when incised, are found to consist entirely of chalky material, which the knife penetrates with difficulty. These are in all probability healed tubercles, although it is not always possible to differentiate between the healed tubercle and a healed abscess or gumma.

Complications of Pulmonary Tuberculosis.—*Pleuritic Adhesions.*—These are extremely common. When extensive, they diminish the respiratory movements and probably thus facilitate the spread of the tuberculous disease. In fibroid phthisis, by uniting the lung with the wall of the chest, they enable the contracting bands of tissue to draw upon the chest-wall so as to deform the thorax. The adhesions result from pleuritic inflammations secondary to the tuberculosis, but not always themselves tuberculous. The pleuritic adhesions found in tuberculosis pulmonalis may at times be independent of the tuberculosis and subsequent to prior simple pleuritis.

Suppuration and Gangrene.—These two processes depend upon the accidental entrance of septic micro-organisms into a tissue of diminished vital resistance. The appearances are quite typical and need no repeated description.

Empyema.—The occasional discharge into the pleural cavity of pyogenic micro-organisms or tubercle bacilli from subpleural tuberculous lesions not infrequently causes suppuration of the pleura, or *empyema*. The empyema is, however, frequently preceded by pneumothorax.

Pneumothorax.—This results from the rupture of a tuberculous cavity, permitting air to enter the cavity of the pleura. It causes collapse of the lung, with great embarrassment of respiration and compression of the lung. As the escape of air is usually accompanied by the escape of septic organisms, the development of pneumothorax is almost invariably followed by suppuration and forms a pyopneumothorax.

Hemorrhage.—Hemorrhage from the lung—*hemoptysis*—may occur from the oozing of the blood from eroded capillaries, usually situated in the walls of the cavities. It may occur from the direct erosion of a blood vessel of considerable size, but is usually preceded by aneurysmal dilatation resulting from weakening of the walls of the vessel. The hemorrhages are of all degrees of severity—sometimes only sufficient to tinge the expectoration slightly red, sometimes large enough to cause the death of the patient from loss of blood. When large hemorrhages are not fatal, they are usually distinctly detrimental, in that the blood which escapes by way of the air-vessels is sucked back into the bronchioles and air-cells with each inspiratory effort, thus lessening the already diminished breathing space, increasing the amount of effete matter contained within the lungs, and paving the way for the development of any septic and putrefactive organisms that may be present. For this reason hemorrhages are sometimes followed by gangrene of the lung.

Syphilis of the Lung.—Syphilitic disease of the lung is rare. It may be either congenital or acquired. The *congenital form* is by far the more common. Its usual appearance is that known as *white pneumonia*, a form resembling bronchopneumonia.

White pneumonia is characterized by the occurrence of consolidated patches which may unite and form lobar areas of inflammation. The disease is so called because of the whitish or grayish color of the inflamed patches, which are completely consolidated. When examined with the microscope, desquamation of the epithelial cells of the alveoli, similar to that seen in catarrhal pneumonia, is observed. There are marked infiltration of leukocytes and a characteristic proliferation of cells in the interalveolar tissue. The blood vessels of the alveolar walls show thickening of the intima. In the lung tissue immediately surrounding the patch there is imperfect development or expansion of the organ. The tissue is always anemic, and its whiteness probably depends in large part upon the anemia. The disease is usually bilateral.

Considerably rarer is the *acquired form* of pulmonary syphilis. Of the syphilitic manifestations, the *gumma,* if not the most common, is the most easily recognized. It undergoes the usual cycle of round-cell infiltration, connective-tissue proliferation, coagulation necrosis, and, in the event of recovery, organization. The resemblance of the pulmonary gumma to softening tubercles must not be forgotten, nor must one forget that the tubercle is of extremely common occurrence in the lung, while the gumma is equally rare, especially in adults.

Actinomycosis of the Lung.—This disease is usually secondary to primary infection of some higher part of the respiratory or digestive tract, from which it spreads by the inhalation of the actinomyces fungi. It occurs in the form of a superficial catarrh of the respiratory passages, accompanied by a fetid discharge in which the microscope shows the presence of the fungi. As the disease ascends higher and higher and the parenchyma of the lung is reached, the alveolar tissue of the organ becomes invaded. Granulomata are formed, each surrounded by a zone of catarrhal pneumonia and appearing as small grayish or reddish nodules. These continually augment in number, the lung sooner or later becoming riddled with them. The nodules and their surrounding pneumonic areas may lead to extensive consolidations, and as the consolidated tissue is prone to undergo softening by suppuration and fatty metamorphosis and break down, the nodules soon lead to the formation of numerous communicating cavities filled with the same purulent material that characterizes actinomycotic inflammations in general. While the invasion is in progress and the early infiltrated parts of the tissue are disintegrating, the formation of new connective tissue takes place in the less inflamed surrounding tissue and leads to a partial encapsulation of the disintegrated tissue, so that the actinomycotic lung is not only riddled with holes, but also considerably indurated.

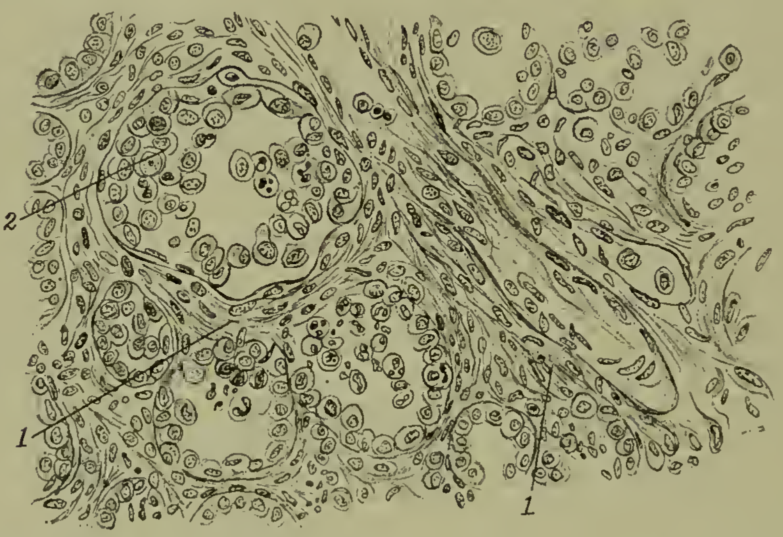

FIG. 282.—Syphilitic "white" pneumonia of the new-born. The alveolar walls are considerably thickened with a richly cellular connective tissue (1). In the alveolar lumen numerous large, desquamated epithelial cells (2) and several leukocytes are seen (× 250) (Dürck).

The disease ultimately reaches the pleura, which becomes covered with the usual exudate and eventually is much indurated and thickened, and often adherent to the chest-wall or diaphragm. By extension through the pleura the disease may extend to the neighboring tissues and invade the muscles of the thorax, the subcutaneous tissue, the skin, the pericardium, the diaphragm, etc.

Glanders.—Glanders of the lung is a rare affection. It is characterized by the formation of small, pea-size, grayish-yellow, whitish or yellowish, cellular nodules. In some cases the disease is rapid and suppurative in form and leads to the formation of rather large-sized areas of pneumonic infiltration, sometimes lobular, sometimes lobar in configuration, and sometimes characterized by the occurrence of hemorrhagic infiltrations.

Lepra.—Leprous lesions of the lung are rare. They have no definite macroscopic features by which they can be differentiated from the other granulomata. The microscope alone can make a positive diagnosis. Tuberculosis of the lung being common among the lepers, care must be taken in making a diagnosis of the condition.

Tumors of the Lung.—Primary tumors of the lung are of comparatively rare occurrence. *Fibroma*, *osteoma*, *lipoma*, *chondroma*, and others have been seen. *Primary carcinoma* of the lung is very rare. It most frequently develops from the mucous glands of the bronchi, and grows with the formation of ragged, fungous, intrabronchial masses which increase in size and extend along the tubes in both directions until they invade the alveolar tissue. Ultimately the distribution takes place through the lymphatics and blood vessels. In some cases the carcinoma may develop from the alveolar epithelium itself and spread from the very beginning through the lymphatics, as well as through the air-system.

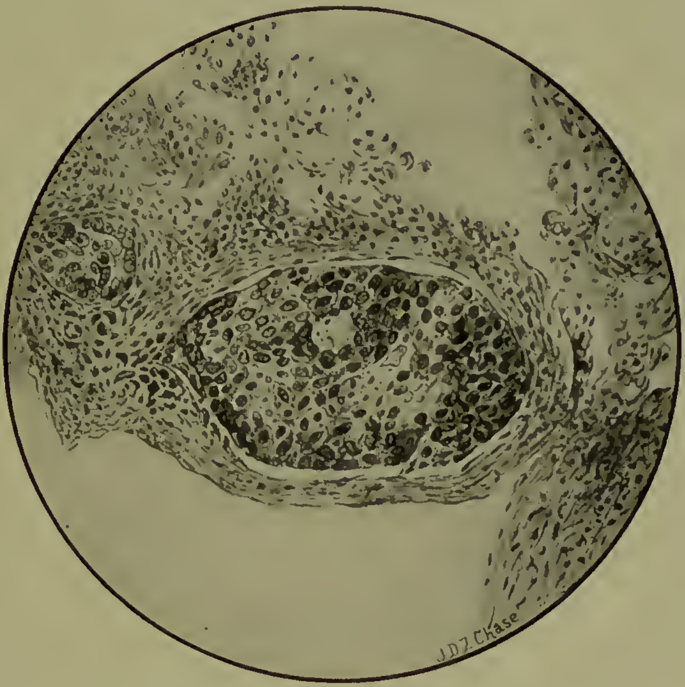

FIG. 283.—Metastatic sarcoma of the lung; a sarcoma embolus in one of the small veins (× 135).

The difficulty of differentiating between the two modes of origin after the lesion has been in existence for a time must be apparent.

The growth of the primary carcinoma is always slow, and its tendency seems to be to remain a circumscribed, though not encapsulated, growth.

The secondary tumors of the lung may be of any metastatic variety. They are usually differentiated from the primary tumors by the number of centers from which they grow. All the secondary tumors are commonly bilateral. The form usually assumed is that of more or less rounded nodes, quite sharply circumscribed from the surrounding tissue. They originate as emboli which lodge in the blood vessels, and, extending through the limitations of the circumscribing vessel, distribute their cells through the lymphatics. It does not follow of necessity, though it often happens, that the growth of the tumor is accompanied by more or less inflammation, which aids in the process of consolidation. The disease spreading along the lymphatic vessels soon extends to the pleura, upon the surface of which little lines of invaded lymphatics can often be seen.

Sarcoma is a frequent metastatic tumor in the lung. Carcinoma is not uncommon.

Bony deposits in the connective-tissue trabecula of the lung are sometimes observed. They are small, numerous, and scattered throughout both lungs. Each mass is irregularly branched in shape, and situated deeply in the pulmonary tissue, where it feels to the examining fingers like a hard nodule. Their intimate attachment to the surrounding connective tissue makes it difficult to remove the masses.

Parasites of the Lung.—Of the vegetable parasites, the *aspergillus*, the *mucor*, and the *oïdium* may be mentioned. They are rarely met, and produce inflammatory changes devoid of any essential characteristics. Among the animal parasites the *Paragonimus Westermanii*, *lung fluke*, or *bronchial fluke*, is occasionally met with in Asia. It becomes encysted near the root of the bronchi, and discharges its eggs into the mucopurulent secretions caused by its presence there. Thousands of these eggs are expectorated every twenty-four hours. It causes hemoptysis.

The *Cysticercus cellulosæ* sometimes becomes encysted in the lungs. The *Strongylus longivaginatus* is occasionally seen. *Monas* and *cercomonas* are mentioned by Ziegler. *Coccidia* and *psorosperms* are also upon record as pulmonary parasites.

The most important parasite of the lung is the *echinococcus*. It is more frequently secondary than primary, and usually depends upon primary disease of the liver. Hence it is most common in the neighborhood of the liver—that is, in the lower lobe of the right lung. The entrance of the parasite into the lung may depend upon the penetration of the diaphragm, or may be due to its distribution through the hepatic vein, inferior vena cava, and right side of the heart. There may be but one parasitic cyst or there may be several in different parts of the lung. The size varies from a walnut to a man's head. When large, they not infrequently cause displacement of the thoracic viscera. In extreme cases they have been known to produce curvature of the spine. The presence of the parasites may cause no inconvenience to the patient, as it often undergoes a natural cycle of changes that ends in a more or less perfect recovery by calcification and encapsulation.

In less favorable cases they progressively increase in size until a time comes when the cyst must rupture. If the cyst ruptures into the pleural cavity, it may cause pneumothorax. If it ruptures into a bronchus, the fluid may be expectorated. In some cases the cyst will suppurate and lead to secondary infections. A case of echinococcus of the branches of the pulmonary artery has been reported by Scheuthauer, and a still more remarkable case, in which the parasite occurred in the lymphatic vessels, has been observed by Virchow. When fragments of the cyst-wall are found in the expectoration, the diagnosis of the condition is made quite easy. The fragments have the well known, milk-white, glassy appearance, cartilaginous consistence, and characteristic disposition to curl up with the free edges inward. The contents, where they can be secured by aspiration or by evacuation, may be allowed to sediment, and then be examined with the microscope for the characteristic hooklets.

DISEASES OF THE PLEURA.

The protected position and simple structure of the pleura combine to lessen the number of primary affections to which it is subject. On the other hand, however, its proximity to the pulmonary tissue and its rich lymphatic circulation favor the development of secondary diseases, the great majority being secondary to disease of the lung.

Active hyperemia is observed as the early stage of pleuritis.

Passive hyperemia most frequently depends upon venous engorgement from obstructive heart-disease. The vessels are distended, and a watery transudate collects in the pleural cavities, causing what is known as *hydrothorax*. Except in pathologic conditions, in which some previous disease has occluded all or part of one cavity, hydrothorax is a symmetric bilateral affection, characterized by the occurrence of a watery, straw-colored fluid in the pleural cavities. This fluid is of low specific gravity and usually does not coagulate spontaneously.

Passive hyperemia also occurs when effusions of the pleura are suddenly removed by aspiration and the pressure upon the vessels is thus relieved.

Hemorrhage.—Petechiæ appear upon the pleura in many of the infectious diseases and in some of the intoxications. They also characterize such ill-defined diseases as scorbutus and morbus maculosus Werlhofii. In the latter diseases rather large ecchymoses are sometimes observed. In death from suffocation the violent inspiratory efforts may so strain the capillaries that they rupture and form subpleural ecchymoses. Large hemorrhages may be caused by the intrapleural rupture of aneurysms, rupture of the lung, lacerated and incised wounds of the chest-wall, fractured ribs, etc., and also from malignant tumors of the pleuræ.

The blood that escapes into the pleura usually fails to coagulate, being in contact with normal endothelium. When not infected, it is slowly absorbed, but its presence is commonly succeeded by agglutinative inflammatory changes in the membrane, with adhesions.

Infection of hemorrhagic extravasations by bacteria entering through the chest-wall or from the lung is serious, leading to purulent and sometimes fetid processes that may prove fatal.

Pleuritis, Pleurisy, or Inflammation of the Pleura.—Pleuritis may be either primary or secondary. As knowledge of the subject advances, the number of primary or idiopathic cases diminishes, and the number of secondary cases increases.

Etiology.—Primary pleuritis is nearly always infectious, but sometimes seems to depend upon exposure to cold, upon sudden chilling of the body, and upon other hygienic indiscretions associated with physical weakness. It sometimes occurs as a complication of Bright's disease and rheumatism, either because of the toxemia or infections that occur in those diseases.

Secondary pleuritis may depend upon the invasion of the pleura by continuity of tissue or by lymphogenic or hematogenic metastasis. In punctured and incised wounds of the chest bacteria introduced by the injurious agent may cause infection and pleuritis. Abscesses of the chest-wall, mediastinum, liver, or other contiguous parts of the body may invade the pleura, either by continuity or rupture. Carious ribs with tuberculosis or other infections may also cause pleuritis. Abscesses, gangrene, tuberculosis, actinomycosis, and pneumonia all involve the pleura either by continuity or by lymphogenic metastasis. In septicemia, pyemia, typhoid fever, influenza, and other infectious processes hematogenic metastasis may cause pleuritis; and in infectious diseases which do not become generalized, local lesions may permit the entrance of bacteria into the circulation, from which they may be conveyed to the pleura, causing pleuritis.

Toxic conditions may also lead to pleuritis, though at present there is little positive knowledge upon this subject.

Bacteriology.—There is no specific bacterium of pleuritis; any irritating organism that accident brings to the tissue may operate injuriously upon it. Thus, abscesses of contiguous parts with secondary invasion of the pleura may furnish staphylococci or streptococci; abscesses or inflammations originating in the alimentary apparatus, the colon bacillus; external traumatic injuries, the pyogenic cocci, the Bacillus proteus vulgaris, Bacillus pyocyaneus, etc.; carious ribs and vertebræ and tuberculous cavities and lesions of the lung, the tubercle bacillus, together with contaminating organisms accidentally present; fetid processes in the lungs, a variety of saprophytic organisms.

Morbid Anatomy.—Pleuritis may be local or general. *Local pleuritis* occurs in traumatic injuries and in local lesions of the pleura. *General pleuritis* involves the whole membrane and probably indicates that the general resisting power of the individual is diminished, or that the virulence of the infecting organism is exceptionally great. The inflammation always begins with hyperemia characterized by a dulness and a redness associated with a slight roughness, the parietal and visceral surfaces ceasing to glide over one another as usual, and their movements being accompanied by pain to the patient. In a short time flakes of fibrin begin to appear upon the surface. This fibrin is probably in part due to an exudation from the blood vessels, in part to a fibrinoid degeneration of the subendothelial connective tissue of the pleura, so that some of the fibrin appears upon the surface, and some is beneath the endothelial layer, which continues for a time intact.

These changes occur in the same manner whether the pleuritis be local or general. The fibrinous exudate serves to make the pleural surfaces adhesive, and in local disease they agglutinate at the injured point, thus checking the painful sliding movement and facilitating repair by holding the parts quiescent.

From this point the inflammation may progress toward recovery or further exudation may occur.

The dry pleurisy described is known as *pleuritis sicca;* pleurisy with exudative effusions, as *pleuritis exudativa.*

Exudative pleurisy is usually general, not local. It may be serous, bloody, or purulent.

The majority of cases are serous and may terminate as such, or may, by subsequent changes, become purulent.

In ordinary *pleuritis exudativa serosa* the dulness and congestion of the membrane characterizing the inception of the inflammation are in a few hours succeeded by the exudation of fibrin. In a length of time varying from a few hours to several days a copious and rapid exudation of serous fluid occurs, and may be so extensive as completely to fill the cavity and rise to the altitude of the clavicle. The lung is compressed upward and backward by the fluid. The pain disappears, but is replaced by dyspnea. The fluid is clear and straw-colored, its specific gravity being about 1.020. It contains 3 per cent. or more of albumin, usually numerous flocculi of fibrin held in suspension, and when aspirated, not infrequently spontaneously coagulates in the bottle.

Should the pleural cavity be opened and inspected, it is found filled with clear fluid, except that the lowest part also contained considerable gelatinous fibrin which has separated from it by coagulation. The surfaces of the pleura appear dull, and show a varying quantity of fibrin adhering to them. Should recovery begin at this point, restitutio ad integrum is not difficult, as it is a simple matter for the fluid to be absorbed. The remaining fibrin is, however, a source of trouble, as it remains long after the absorption of the serum and may form a temporary support upon which new connective tissue and vascular loops grow, forming *adhesions* or fibrous unions between the approximated surfaces. How long the surfaces of the pleura, once inflamed, remain roughened and irregular is difficult to determine, but those who have suffered from pleurisy can testify to the fact that disagreeable sensations in the chest, depending upon the irregularities and adhesions, remain for years.

The extent of adhesion varies considerably. Sometimes the entire pleural cavity is obliterated; sometimes the adhesions form pockets here and there; sometimes they are only occasional and of limited extent. Adhesion of the pleura from local inflammations appears to be very common: fully 80 per cent. of the autopsies I have held have shown old fibrous adhesions at the apices or external surfaces of the lungs.

When a second attack of pleurisy occurs in one who has pleuritic adhesions, the exudation may occur only in the occasional pockets—*loculated* or *sacculated pleurisy*.

When the infection of the pleura is exceptionally virulent, the serous effusion may change to pus, or a pleurisy may be purulent from the beginning. Purulent pleurisy is known as empyema.

Empyema.—Thoracic empyema, or purulent pleurisy, is an infectious inflammatory condition of the pleura characterized by a purulent accumulation in its cavity.

Etiology.—It is always infectious, but not specific, as a variety of micro-organisms may cause it. It may follow traumatic injuries of the chest-wall, local disease of the chest-wall and lung, lymph metastasis, and blood metastasis.

Traumatic Injuries.—In most cases it is easy to explain empyema after traumatic injuries of the chest-wall if one finds an external or pulmonary wound through which the infectious agent could enter. Such lesions are evident in punctured and gunshot wounds, compound fracture of the ribs, hypodermic and paracentesis wounds, etc. In some few cases, however, it is difficult to see how the trauma acts. This is well illustrated in a case mentioned by J. G. Sutton,[1] who speaks of having "performed an autopsy upon the body of a young muscular man who died rapidly from suppuration of the pleura after a blow on the side. There were no other lesions."

A traumatic non-specific purulent pleurisy may be experimentally produced by the introduction of irritating chemic substances—oil of turpentine, etc.—into the pleural cavity. In the traumatic empyemas the cause of infection seems to enter the chest from without, and examination of the pus in such cases usually reveals the presence of staphylococci and other familiar micro-organisms.

In speaking of chest-punctures as causes of empyema some mention should be made of the exploration of the chest by the hypodermic needle and the withdrawal of fluid through an aspirating needle as sources of infection. Griffiths[2] in 1887 carefully studied 151 cases of aspiration and found that in 2 cases only did the fluid become purulent. One of these was complicated with tuberculosis, the other with erysipelas.

Local disease of the tissues contiguous to the pleura is a fruitful source of empyema. Bronchopneumonia, especially occurring in influenza and tuberculosis; croupous pneumonia, tuberculosis, carcinoma, gangrene, cavity and abscess formation of the lung may lead to empyema under appropriate conditions.

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[1] *Lectures on Pathology*, p. 235.

[2] *British Medical Journal*, 1887, vol. i., p. 831.

In tuberculosis, which is the most fruitful source of the disease in adults, the tuberculosis itself may excite empyema, the condition having been observed in primary tuberculosis of the pleura as well as in tuberculosis of the lung, or the disease may lead to empyema through the escape of infectious material from small superficial cavities. If these cavities rupture, pneumothorax usually results. In tuberculosis it is possible for empyema to depend upon extension of the infection along the lymphatic channels from lung to pleura, but this seems to be quite rare, for in tuberculous empyema the tubercle bacillus is commonly the only micro-organism present, and not infrequently careful search fails to discover any organisms in the pus. The tuberculous empyema commonly develops as a serofibrinous pleurisy which subsequently becomes purulent.

Carious ribs and vertebræ sometimes lead to empyema, though probably more frequently the reverse condition is true and the empyema leads to caries and necrosis of the bone.

Perforation of the diaphragm and the evacuation of a hepatic abscess into the pleural cavity have been known to excite empyema. Carcinoma of the esophagus and even of the stomach may, by perforation into the pleural cavity, cause purulent inflammation.

The rupture of echinococcus cysts and the escape of their contents into the pleura may lead to pus-formation.

Sometimes mediastinal abscesses and suppurating or tuberculous bronchial or mediastinal lymphatic nodes break down and evacuate into one or the other pleural cavity, with resulting empyema. In rare cases gumma of the lung, liver, pleura, chest-wall, or other tissue may, by rupture or otherwise, act as exciting causes of purulent pleurisy.

As in the traumatic empyemas, no one specific micro-organism covers all these cases, and in each particular condition the micro-organisms present are easily accounted for by the primary condition.

Lymphatic metastasis is probably an important means by which bacteria reach the pleura from neighboring but not contiguous tissues. In some cases it may be that primary inflammatory diseases of the pericardium extend to the pleura through the lymphatics. It may be by the lymphatics that the pleura becomes infected in pneumonia. Sometimes the source of infection seems to be much more remote. Sutton mentions the occurrence of pleurisy in middle-ear disease by extension of the inflammation to the cellular tissue of the pleura along the sheath of the jugular vein. Wounds of the neck and ligations of the great vessels of the neck have been followed by pleurisy of similar origin.

In rare cases peritonitis may extend to the pleura by lymphatic extension through the diaphragm.

Blood metastasis is typically illustrated by pyemia. The bacteria circulating in the blood may be deposited directly in the pleura with the production of small abscesses which open into the pleura and infect it, or there may be a previous hematogenic septic pneumonia with miliary abscesses and escape of bacteria into the pleura. In some of the infectious fevers empyema occurs either as a complication or as a sequel. This is most frequent in scarlatina, but also occurs in typhoid, measles, whooping-cough, and pneumonia. The micro-organisms present may or may not be those specific for the respective diseases.

In diseases characterized by diminished resistance to infection, as nephritis, the micro-organisms which enter the blood and fail to meet with prompt destruction may accidentally lodge in the pleura and excite empyema.

Bacteriology.—The bacteria most frequently discovered in the pus of empyema are the streptococcus, pneumococcus, tubercle bacillus, staphylococci, typhoid bacillus, influenza bacillus, Friedländer's bacillus, and Bacillus coli communis.

The micro-organisms found in the pus vary considerably with the time of life at which the empyema occurs. Thus in children the pneumococcus is most frequently met, while in adults it is the streptococcus. In adults the number of tuberculous empyemas is nearly twice as great as in children. Netter found the following micro-organisms in empyema:

	Children.	Adults.
Pneumococcus	53.6	17.3
Pneumococcus and streptococcus	3.6	2.5
Saprophytic organisms	10.7	
Staphylococci	. .	1.2
Tubercle bacillus	14.3	25.0
Streptococci	17.6	53.0

Gonococci, colon bacilli, Friedländer's bacillus, typhoid bacilli, and influenza bacilli have been found in empyema pus. Osler says that occasionally psorosperms have been found. Spirilla were unexpectedly encountered in one case, and corresponded with the form frequently met with in the mouth. They could not be cultivated. A case of leptothrix empyema in a dog is on record.

Diphtheria bacilli have been found in empyema occurring as a sequel of diphtheria, though usually the streptococcus would be expected in these cases.

Putrid empyema is caused by the entrance into the pleural cavity of saprophytic bacteria. The condition usually occurs in cancer of the gastro-intestinal apparatus, from micro-organisms which work their way into the mediastinum and gradually invade the pleura, or from gangrene of the lung. The pus is characterized by extreme fetor.

The bacteriologic flora is very mixed, many species, both aërobic and anaërobic, being present.

Würz points out that considerable practical prognostic importance attaches to the bacteriologic study of the pus of empyema. Thus empyema in childhood, caused by the pneumococcus, is quite benign and runs a rapid course to recovery, while that caused by the streptococcus runs a slower course and is more serious. Tuberculous pleuritis is a chronic process usually terminating fatally or lasting for years until tuberculosis or an intercurrent affection carries off the patient or he gradually succumbs to prolonged hectic, amyloid disease, or asthenia.

Empyema is more frequent in children than in adults. Mackey found that 40 per cent. of the pleural effusions of childhood but only 5 per cent. of those of adults were purulent. The disease may occur at any age. Pleuritis has been found in the fetus and in the new-born. The greatest number of cases in adults occur between the twentieth and fiftieth years.

The affection is usually unilateral, though both sides may be affected. The left side is more frequently affected than the right.

Morbid Anatomy.—The pleural cavity contains pus, the quantity varying from a few cubic centimeters to several liters, and the quality according to the mode of formation and duration.

In the cases which begin with a serofibrinous exudate and later develop into empyema the formation of pus is indicated by a clouding of the liquid. Later the great increase in the corpuscular elements gives the exudate the typically purulent appearance. In these cases the amount of exudate is usually considerable before it becomes distinctly purulent.

In the cases which are purulent from the beginning pus-formation may be observed at any stage, and the quantity of pus first discovered may be very small. In ordinary cases there is a distinct tendency for the pus to separate into layers through the sedimentation of the contained corpuscles. This leaves a fairly clear fluid, with a thick, crumbly or flocculent sediment below. Errors in diagnosis may be occasioned by this sedimentation, as unless care be exercised, an exploring needle may withdraw clear fluid only.

The appearance of the pus varies with different conditions and in the different infections. The pus in the pneumococcus empyema of children is apt to have a greenish color. In the ordinary streptococcus empyema of adults it presents the appearance of laudable pus. In the tuberculous cases it is somewhat variable, though usually flocculent and curdy and lacking in healthy morphologic constituents.

The pus has a specific gravity varying from 1.023 to 1.015. It is, of course, rich in albumin and contains glycogen, paralbumin, urea, uric acid, and cholesterin (Naunyn). Sometimes leucin, tyrosin, and xanthin are present. In rare cases crystals similar to those of spermin are present, and are thought by some to indicate that the empyema originates from ruptured hydatid cysts.

The pus usually has an acid reaction, but if infected by saprophytic micro-organisms, may become alkaline.

The progress of the disease is frequently associated with changes in the exudate. In individuals with good absorbing powers, as in children, it is possible for the entire exudate to be absorbed. In the greater number of cases, and especially in adults, however, the fluid is absorbed, leaving the corpuscular elements to undergo subsequent degenerative changes. Fatty degeneration, the formation of fatty acids, leucin, tyrosin, cholesterin, etc., take place in the corpuscles, and the inspissation of the solid part of the exudate by the absorption of the fluid changes the contents of the pleural cavity into a cheesy or crumbly mass of grayish-yellow color. In the course of time lime-salts usually precipitate in this mass, which then becomes dense and gritty.

Changes in the Pleura.—In pneumococcus empyema of children the pleura may show surprisingly little alteration, its surface being smooth and shining or slightly dulled and congested. Upon microscopic examination the subendothelial tissue of the pleura is found infiltrated wlth pus-cells.

More completely in empyema the pleura participates in the disease process, and upon its congested and thickened surface flakes of fibrin and shreds of degenerating endothelial tissue are observed. As the empyema continues to increase in size and the pus to act upon and macerate the tissue, the pleura may become more and more distinctly covered with a grayish-white loose pseudomembrane. When stripped off, this sometimes leaves a shining surface, which indicates that the endothelium is intact, but more frequently leaves a dull, eroded surface, which indicates that the endothelium is destroyed. The nature of the pseudomembrane is uncertain. It is thought by most pathologists to originate from the inflammatory exudate by coagulation upon the surface. By others it is looked upon as a product of the degenerating endothelium; by still others, who find that the endothelium is sometimes elevated and covers the so-called fibrin formation, as a product of subendothelial connective-tissue degeneration of the pleura.

In many cases of empyema pleuritic adhesions are observed. They probably depend in a majority of cases upon antecedent troubles. Their formation usually begins at the apices of the diseased lungs, probably because of the quiescence of that part of the pulmonary tissue during respiration, and because the accumulating exudate separates the surfaces lower down.

The adhesions may be inconspicuous, but frequently descend nearly to the fluid, which becomes circumscribed, so as more closely to resemble an abscess cavity than a purulent collection in the pleural cavity. The corroding action of the pus upon the pleura is quite evident, and from prolonged contact it loses the endothelial covering, becomes greatly thickened, infiltrated with pus-cells, and forms a true "pyogenic membrane."

In this thickened and altered pleura lime-salts are deposited earlier than in the inspissated pus of the cases terminating by absorption, and sometimes true bone-formation—pleural bones—has been observed.

The pulmonary pleura is even more diseased than the costal pleura, so that in chronic cases the lung becomes covered with a thick rind which is soft, edematous, necrotic, and lacerable so long as there is fluid in the chest, but which transforms into an unyielding callous rind when evacuation or absorption brings about regenerative changes.

Changes in the Lung.—It is almost impossible for empyema to occur without incommoding the action of the lung, and except in the benign pneumococcus empyema of childhood and possibly a few of the rapid streptococcus empyemas of adults, they cannot occur without leaving permanent changes in the lung. The chronic tuberculous empyema is particularly damaging to the pulmonary tissues.

The immediate effect of empyema is to occupy space, so that complete expansion of the lung becomes impossible. As the empyema becomes larger the expansion becomes less and less, until atelectasis is almost complete and in exaggerated cases the organ becomes inconspicuous in size, flattened in form, and may later not only be atelectatic, but also compressed by the increasing fluid. The tissue is solid, airless, tough, leathery, and grayish or reddish-brown or even blackish in color. When incised, it is non-crepitant and carnified. The bronchial tubes may appear larger than normal and may contain mucopus.

Few cases reach such a stage of compression and destruction as this, partly because few empyemas become large enough, and partly because of the early formation of adhesions between the pulmonary and costal pleuræ in the upper part of the chest. If pus forms after adhesion, a *loculated empyema* may result.

When the chest cavity is opened in cases of empyema, the lung may not appear and the empyema may seem to occupy the entire pleural cavity. This appearance depends upon the fact that adhesions have formed between the lung and less diseased parts of the pleura, while over the exposed pulmonary and costal surfaces the macerated, thickened, and infiltrated pleura is completely changed into a "pyogenic membrane."

In still less marked cases, when adhesions are not extensive and the processes less chronic, the surface of the pleura becomes infiltrated and thickened, and in the repair that follows the thin edges of the lung suffer most.

In chronic empyema the macerating and corroding effect of the pus is exerted in large measure upon the pulmonary pleuræ, which sometimes become so softened and infiltrated that the pus is permitted to enter the alveolar structure of the lung without actual perforation and be expectorated. That this process is one of infiltration and does not depend upon perforation is shown by the fact that in these cases pneumothorax does not occur.

The absorption of the pus and its entrance into the lymphatic structure of the lung are followed by inflammation of its interstitial tissue, so that pleurogenic pneumonia usually occurs. If this process is active, the dissecting effect of suppuration is very marked; if chronic, the fibrosis predominates and the trabeculæ of the lungs are thickened.

The recovery of empyema is followed by further disaster to the pulmonary tissue by the fibrosis that takes place. In mild cases of moderate duration the thickened pleura, by its contraction, rounds off the sharp inferior edges of the lung and offers some impediment to complete expansion. In bad cases the expansion is greatly or completely hindered by the firm callous rind of almost cartilaginous consistence which forms upon the compressed lung.

In chronic, exaggerated cases, atelectasis, carnification, fibrosis, and calcification all coöperate to make any improvement in the condition of the lung impossible.

When such cases recover or improve after evacuation, the lung is unable to expand and occupy its normal position, so the ribs fall, the side sinks in, and a marked deformity of the thorax follows.

Empyema with atelectasis and compression of one lung is always accompanied by vicarious action of the other, whose tissues are more or less inflated in consequence. In breathing exercises directed toward the expansion of the diseased lung it is the sound lung that is chiefly influenced, and care should be taken not to have the inspiratory efforts so forcible as to occasion emphysematous changes in it.

Changes in the Thorax.—The formation and continuance of empyema are accompanied by enlargement of the affected side. The diameter of that side is greater than that of its fellow, and the intercostal spaces bulge. The diaphragm is pushed down, and with it the liver on the right side or the spleen on the left. The heart is usually dislocated toward the opposite side, and may embarrass the movements of the normal lung.

After evacuation and recovery the affected side of the chest usually collapses, the ribs sink in, the shoulder droops, and the spinal column makes a scoliotic twist toward the empyemic side.

The hope of improvement by gymnastics will often be defeated by the further contraction of the new fibroid tissue in the chest, and all hope of causing the lung to expand in exaggerated chronic cases may as well be abandoned.

Effect upon the Respiration.—The empyema, with the collapse of pulmonary tissue which it involves, is an important hindrance to respiration, so that dyspnea and insufficient aëration of the blood are usual. In addition to the compromised breathing-space on the diseased side, the dislocation of the heart toward the other side increases the difficulty, and from the time the empyema forms, it becomes a source of respiratory deficiency. The described subsequent changes make it impossible for this ever to be overcome, and the patient will remain a more or less feeble breather. In some cases, especially in children, the dyspnea may be so slight, however, as to escape observation.

Effect upon the Circulation.—The dislocation of the heart by pressure of the accumulating pus is noticeable in most cases, and the pressure often transmits the cardiac impulse to the purulent accumulation and occasions *pulsating empyema.*

The dislocation of the heart also makes traction upon and may kink the great vessels, especially at the diaphragmatic orifices, so that the circulation in the lower extremities is disturbed and may show itself in venous congestion.

General disturbance of the venous circulation is also occasioned by the obstruction of circulation in the diseased lung and increased labor of the right side of the heart. Right-sided cardiac hypertrophy is not infrequently observed in consequence of this increased labor.

The disturbed pulmonary circulation, as has been pointed out by Orth, is not infrequently associated with compensatory venous collateral communications between the pulmonary vessels and those of the thoracic walls.

Course and Termination.—Contact with the pus not only affects the pleura, but seems to affect the subjacent tissues as well. We find the tone of the muscles is lost, so that in empyema the diaphragm is more depressed than in other fluid accumulations in the chest, and the intercostal muscles indicate loss of tone by permitting the spaces to bulge.

The erosions sometimes progress so that the subpleural and deeper tissues are destroyed, and the empyema, like other abscesses, "burrows" its way to the surface to evacuate. This form is described as an *empyema necessitatis.* Such an empyema usually "points," and if not surgically treated, spontaneously evacuates its contents. By the greater number of writers it is said that the "pointing" and evacuation usually take place, as was first pointed out by Cruveilhier, in the space between the sternal end of the lower costal cartilage and the sternal border, the reason given for this being that the external intercostal muscle is absent and resistance diminished. Eichhorst found that in nearly all his cases the perforation of the chest-wall took place in the fifth and sixth intercostal spaces between the mammary and axillary lines. Osler says the perforation of the chest-wall may occur anywhere from the third to the sixth interspace. According to Marshall, it is usually in the fifth. While distinctive enough, the burrowing and pointing of an empyema may become most perplexing by making its appearance in unusual places. Eichhorst mentions a case in which the pus burrowed down behind the peritoneum and suggested a paranephritic abscess. Cases are not lacking in which it descended to Poupart's ligament and simulated psoas abscess. It has been known to reach the knee before pointing. Bouveret described a case that pointed in the lumbar region and simulated a lumbar aneurysm.

Spontaneous rupture is usually sudden, and a liter or more of pus may escape with a gush. In some cases, however, the opening is very small and the pus escapes in drops.

The evacuation may take place from a single opening or there may be several, which may communicate beneath the skin. In a few cases evacuation is followed by closure of the fistula and recovery, but the majority of cases exhibit fistulous communications with the chest, remaining for years. Osler mentions a case given in Copeland's *Dictionary of Medicine*, of a Bavarian physician who had a pleural fistula for thirteen years and enjoyed fairly good health.

As long as the fistula remains open it continues to discharge pus, and the drain upon the system thus incurred ultimately may lead to constitutional involvements, such as amyloid disease, of which complication the patients may die if not carried off in advance by the tuberculosis occasioning the cold abscess or by intercurrent affections.

The erosions caused by empyema are always exerted upon the external tissues, and their movement and evacuation are not always toward the outer surface of the body. Sometimes the lung is eroded and a fistulous communication with a bronchial tube set up. This is a dangerous accident, as the patient may aspirate pus into the healthy part of the lung, and drown in it. When this does not happen, pneumothorax is nearly always sure to follow.

Sometimes the perforation occurs into the esophagus or into the stomach, and the pus is vomited or passed with the feces. The pericardium is sometimes perforated. The mediastinum is not infrequently involved, and an empyema of one side may find its way to the opposite side by fistulas through the mediastinum.

The presence of pus in the pleural cavity gives rise to more or less well-marked constitutional symptoms, such as loss of appetite, hectic fever, and sweats, and there is always pain of greater or less intensity in the affected side. So soon as the pus is evacuated, these symptoms subside. If, however, the fistula heals and pus reaccumulates, the symptoms again make their appearance.

Pneumothorax, or air in the cavity of the pleura, is the result of accidents which almost invariably lead to empyema, so that it finds its proper mention in connection with it. The escape of air into the pleural cavity is most frequently dependent upon the rupture of the thinned wall of a superficial tuberculous pulmonary cavity. The air enters the pleural cavity during inspiration, when a vacuum is formed there by the action of the respiratory muscles. Not being inclosed in the elastic alveolar tissue of the lung, however, and not being forced by the contracting air-cells into a series of conducting tubes facilitating its escape, the air remains in the chest and acts as a cushion, compressing the lung during expiration. With each inspiration more air enters until the air-pressure within and without the pleural cavity is equal, after which it acts as a constant embarrassment by compressing the lung and preventing expansion.

Pneumothorax is not only a serious accident, because of the difficulty in breathing but also because it usually adds an infection which soon transforms it into a pyopneumothorax.

Etiology.—It may result from external perforating wounds of the chest, as by foreign bodies or broken ribs; from accidental perforations of the esophagus or stomach into the pleura; rupture of the lung from violent crushing of the chest; and has been known to occur in consequence of the invasion of the pleural cavity by gas-producing bacteria, such as the *Proteus vulgaris*, under which circumstances the pneumothorax may develop without any communication with the external air.

Pneumothorax is very rarely a collection of gas only; nearly always a collection of fluid is present in the chest, which, according to its quality, causes the conditions described as *hydropneumothorax*, *hematopneumothorax*, *seropneumothorax*, *pyopneumothorax*, etc.

Pyopneumothorax is a condition in which both air and pus fill the chest cavity; it adds to the inconveniences of the pneumothorax the more serious suppuration. If, before the development of pneumothorax, extensive adhesions between the chest and lung shall have been formed through previous attacks of pleuritis, the lung may be able to continue respiration because of the expansive traction of the respiratory movements. When complete union of the costal and pulmonary pleuræ has occurred, pneumothorax is impossible.

Weil divides pneumothorax into—

1. *Open pneumothorax*, in which the air has free entrance and exit through the perforation.
2. *Ventilated pneumothorax*, in which the opening is so situated or so shaped as to permit the air to enter during inspiration, but not to escape during expiration. The air ceases to enter when the maximum pressure is attained.
3. *Closed pneumothorax*, in which the opening, having permitted air to enter the pleural cavity, closes by actual healing or by fibrinous plugging, and no communication any longer exists.

In tuberculosis with large or superficial cavities the exciting cause of the development of the affection is usually some strain, as a violent cough, etc.

At the autopsy the chest is found distended, and as the knife enters to sever the costal cartilages, the air often rushes out with an audible sound. At times, instead of air, an inflammable gas may escape. The lung is always found to be more or less compressed, according to its condition (consolidated lungs cannot be compressed). In most cases there is serofibrinous, purulent, or other fluid in the chest cavity, and upon inspection the perforation from which the air escapes can usually be found. They are more frequently situated in the upper lobe than in the lower, probably because cavities are more common in the upper lobe. When in the lower lobe, they are most common posteriorly at the apical portion.

Chylothorax is a rare affection, of which but few cases are upon record. It usually occurs in consequence of injury or disease of the thoracic duct. The fluid that collects within the chest is of milky appearance, and is said to yield a layer of creamy fat when allowed to stand.

Tuberculosis of the Pleura.—Primary tuberculosis of the pleura is rare. It usually occurs in the form of clusters of rounded, pearly masses about the size of a pea (*pearl disease*). From these the miliary tubercles may be seen extending along the lines of the lymphatic vessels. Secondarily it results from the extension of tubercular affections of the ribs and spinal column to the pleura. It may also be of secondary, hematogenic, metastatic origin as a part of general miliary tuberculosis. It is most common as a secondary affection in pulmonary tuberculosis.

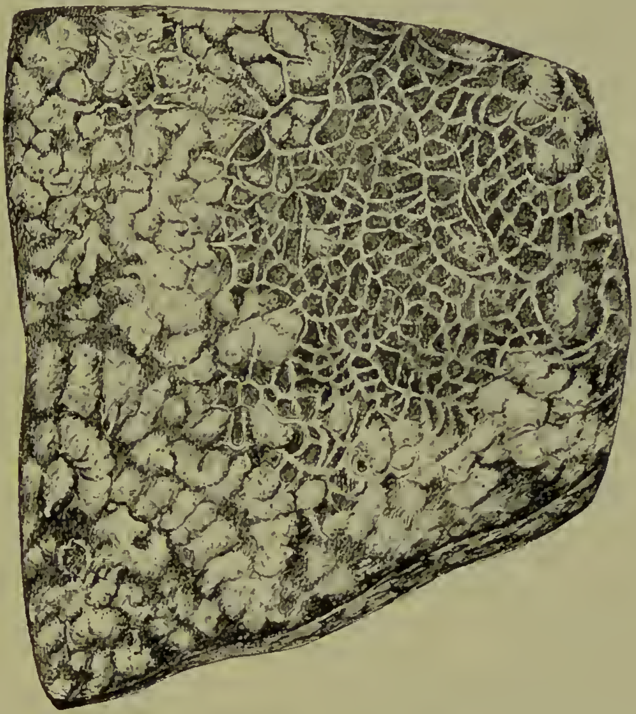

FIG. 284.—Carcinoma of the pleura. Pleuritis carcinomatosa in primary carcinoma of the stomach. The white nodules are lymphogenic metastatic tumors (Bollinger).

It may manifest itself only by the eruption of a few miliary tubercles upon the pleural surface, with a superficial coating of fibrin ; or it may appear as a well-marked affection characterized by wide-spread adhesions between the costal and pulmonary pleuræ ; or, further, it may be of extreme severity accompanied by empyema, in which no other micro-organisms than the tubercle bacilli can be found. The tubercles that develop in the course of the affection are without peculiarities. They spread along the lymphatics of the pleura. Occasionally one finds considerable conglomerations of tubercles with or without caseation.

Tumors of the Pleura.—Of the primary tumors, the most common and the most important is the *endothelioma*. *Fibroma*, *sarcoma*, *angioma*, *lymphangioma*, *lipoma*, and *osteoma* have been observed.

The secondary tumors are more frequent and occur in consequence of metastasis from mammary carcinoma and malignant diseases of the thyroid, stomach, and esophagus.

Parasites of the Pleura.—Echinococcus cysts are occasionally found in the pleura.

Diseases of the Mediastinum.—It is usual to make a brief mention of the mediastinal diseases in connection with the diseases of the respiratory system, because of the anatomic relation of the tissues, and because it so frequently happens that the mediastini suffer from contiguity and continuity in many of the diseases of the bronchi, bronchial glands, and pleuræ.

Mediastinitis is inflammation of the areolar or cellular tissue of the anterior, median, or posterior division of the mediastinum. Like other inflammations, it may be either acute or chronic. The acute form is frequently suppurative ; the chronic, productive. The disturbance is usually traumatic or rheumatic, but may depend upon pleuritis, pericarditis, ostitis, etc.; or may result from the outward rupture of pyopericardium or pyothorax. A *tuberculous mediastinitis* not infrequently succeeds tuberculosis of the lungs and pleuræ. The rupture of enlarged, inflamed, or tuberculous bronchial lymphatic glands also sometimes produces it.

The *course* of mediastinitis does not differ, except as its anatomic relations may affect it, from inflammations of other cellular tissues.

Interstitial mediastinal emphysema is not uncommon in consequence of small globules of air traveling along the trabecula of the lung and its root, in pulmonary emphysema, and as the result of traumatism.

Tumors of the Mediastinum.—The most common primary tumor is *sarcoma*, chiefly lymphosarcoma, which originates from the lymph-glands or cellular tissue of the part. In Hodgkin's disease the posterior mediastinum is not infrequently invaded by the lymphatic tumors.

Osteoma, *fibroma*, *lipoma*, and *chondroma* have also been seen in this location.

Carcinoma is a secondary tumor of the mediastinum. It is usually of rapid development and of the medullary form.

Dermoid tumors are not uncommon in the mediastinum. They may develop from the thymus gland, but are more likely fetal inclusions.

Parasites.—The *echinococcus* is occasionally encountered in the mediastinum.

CHAPTER V.

DISEASES OF THE SKIN.

Active hyperemia of the skin is known as *erythema*. It is a common affection, resulting from slight traumatic injuries, burns of the first degree, the action of irritating substances, excessive cold (*erythema pernio*), combination of warmth, moisture, and friction (*erythema intertrigo*), and precedes inflammation. It also occurs in specific infectious conditions, such as scarlatina and rubella, and in certain vasomotor disturbances.

Hyperemia may be diffuse or circumscribed, the latter often occurring in small, rounded areas and known as *roseola*.

Passive hyperemia in weak heart is characterized by a blueness of the lips, fingers, toes, and other parts, known as *cyanosis*. After death the sedimentation of blood to the dependent parts of the body is the cause of a postmortem condition described as *livores mortis*.

Continued hyperemia is accompanied by some edema and more or less desquamation. Not infrequently some pigmentation remains when the hyperemia has disappeared, depending upon hemolysis following diapedesis. Venous stasis of the veins of the anterior aspect of the leg—*varicose veins*—brings about a condition of connective-tissue thickening, with loss of the vital resistance of the tissues to injury, which is apt to result in what is known as *ulcus cruris* or *varicosum*. Slight injuries with infection lead to large superficial sloughs and ulcerations—leg ulcers.

Hemorrhage into the tissues of the skin frequently occurs in traumatic lesions and in infectious exanthematous diseases, pernicious anemia, purpura, scurvy, intoxications, etc. The blood usually extravasates into the corium or into the papillary layer, and may find its way under the epithelium or between its cells. Hemorrhages are characterized by failure to disappear under pressure and by a red or purple color. They may be divided into *traumatic*, *idiopathic*, and *symptomatic forms*. Idiopathic hemorrhages are usually spoken of as *purpura*. Minute hemorrhages are called *petechiæ*; elongate stripes and branched linear hemorrhagic marks are sometimes described as *vibices*; large hemorrhages, as *ecchymoses*. Sometimes the blood escapes in quantities sufficient to form distinct cystic accumulations, or *hematomata*.

Blood occasionally enters the sweat-glands and escapes with their secretion, causing *hematidrosis*.

Purpura or **peliosis rheumatica** is an affection characterized by the occurrence of small, often petechial, subcutaneous hemorrhages, chiefly distributed over the lower limbs. It usually occurs in rheumatism and rheumatoid disorders, and is probably infectious in nature.

Edema of the skin is usually the result of kidney disease or of increased transudation from the vessels in venous or lymphatic stasis. Edema may be local or general, the term *anasarca* being used to describe the latter condition.

Œdema neonatorum is frequently confused with *sclerema neonatorum*. It is a rare condition seen in children exposed to cold shortly after birth.

Angioneurotic edema is the result of vasomotor disturbances sometimes caused by eating fish, strawberries, mushrooms, etc. It seems to be purely reflex and nervous in origin.

The angioneurotic edema is chiefly characterized by its circumscribed and acute occurrence. It is frequently associated with urticaria, from which it is with difficulty differentiated, especially in cases with very large *wheals.* It begins in the subcutaneous tissue, however, and never follows external irritation.

Anemia of the skin is recognized chiefly by the extreme pallor, induced by the absence of blood. It may be the result of general anemia, or may be local and dependent upon the action of vasoconstrictor nerves, as in Raynaud's disease, or to the action of cold, astringents, etc.

In *pernio,* or exposure to cold, the skin becomes anemic from vasoconstriction.

Pigmentation or melanoderma of the skin may occur locally or may be widely distributed. Of course, the amount of pigment contained in the cells of the Malpighian layer of the skin varies in the different races and in different individuals. Aside from this, however, we have true pathologic conditions.

Local Pigmentations.—*Nevi* or moles are common lesions, sometimes congenital, sometimes acquired. Some are elevated above the surface of the skin (*nævi verrucaci*), while others are not (*nævi spili*). Inasmuch as they are pigmented, they are called *nævi pigmentosi.* They may be as small as a pin-head or large enough to cover several square feet of surface. The surface is frequently covered with hair (*nævi pilosi*). The pigment is found in the cells of both the epidermis and the corium. Similar moles of a yellowish color are called *xanthelasma* or *xanthoma.* Local pigmentations of inflammatory origin not infrequently follow the application of blisters, mustard-plasters, actual cautery, etc., to the skin, and occur after mild burns.

Lentigo, ephelides, or "freckles" are acquired, non-elevated, yellowish or brownish spots of small size, which develop upon the skin of fair individuals in consequence of exposure to the sun.

Chloasma or *melasma* is characterized by larger, yellowish, brownish, or blackish patches, of irregular size and shape, which usually appear upon the face. They are symptomatic, depending upon biliary, uterine, cachectic, and other conditions. They are common upon the forehead in pregnancy and sometimes during menstruation.

Melanosis, Addison's disease, or *melasma suprarenale* is characterized by an acquired, universal pigmentation of the skin. The pigmentation is more marked upon the face and hands. It may cause only a slight darkening and muddy color, may be a distinct bronzing, or may be almost black. The distribution is often rather streaked.

Icterus or *jaundice* is a pigmentation of the skin and deeper tissues by bile. It causes the entire surface to assume a yellow-green or olive color. The bile reaches the skin through the blood.

Argyria is a deposit of chlorid of silver in the skin as the result of prolonged administration of nitrate or other salts of silver.

Ecchymosis is extravasation of blood into the superficial tissues following a contusion or other injury.

Tattoo-marks result from the intentional introduction of insoluble pigments into the epiderm by needle-pricks. Various colors, chiefly carmin and India ink, are employed, the resulting effect usually being some permanent artistic design.

Leukoderma, or absence of pigment from the skin, is seen in its most marked and most typical form in the congenital and occasionally hereditary affection known as *albinism* (*q. v.*) or *congenital leukopathia.* Albinism is, as a rule, universal absence of pigment in the skin. Partial albinism is, however, occasionally observed. *Acquired leukopathia* is known as *vitiligo.* It sometimes occurs spontaneously, sometimes follows such infectious diseases as scarlatina, typhoid, etc. It may be endemic. The skin and hair in the affected areas are entirely devoid of pigment, and appear white, in marked contrast to the normally pigmented skin. An epidemic form of leukoderma or vitiligo is sometimes seen, and is supposed to be contagious and related to leprosy. Leukoderma is a symptom of leprosy, in that the pigment of the skin disappears in many cases from the diseased areas, especially where cicatricial tissue is forming. The hair upon these areas is white and often coarse.

Atrophy of the skin is observed in senility. The skin becomes thin, and the papillæ become short and may disappear. The fibrillar and elastic elements undergo a hyaline degeneration and disappear, the vessels become destroyed, and pigmentary deposits in the form of yellowish granules in the rete Malpighi are observed. The horny layer of the epidermis is scaly, and is separated from the papillary layer by very few layers of cells. The hairs fall and are not replaced because of atrophy of the follicles. Sometimes fine woolly hairs are produced before the atrophy of the root is sufficiently advanced to prevent the growth of hairs. Sometimes the atrophic follicles are obstructed by epidermal accumulations and undergo cystic dilatations, each little cyst containing a hair. The cyst is formed partly by the hair-follicle, partly by the related sebaceous glands, which latter often discharge their secretion into the cyst, so that a considerable size may be attained and a "*wen*" or "*atheroma*" be formed.

Atrophic conditions of the skin associated with exfoliation of the epidermis in the form of fine scabs are spoken of as *pityriasis*. *Pityriasis simplex* is frequent in old age; *pityriasis tabescentium*, in tuberculosis and other chronic marantic affections.

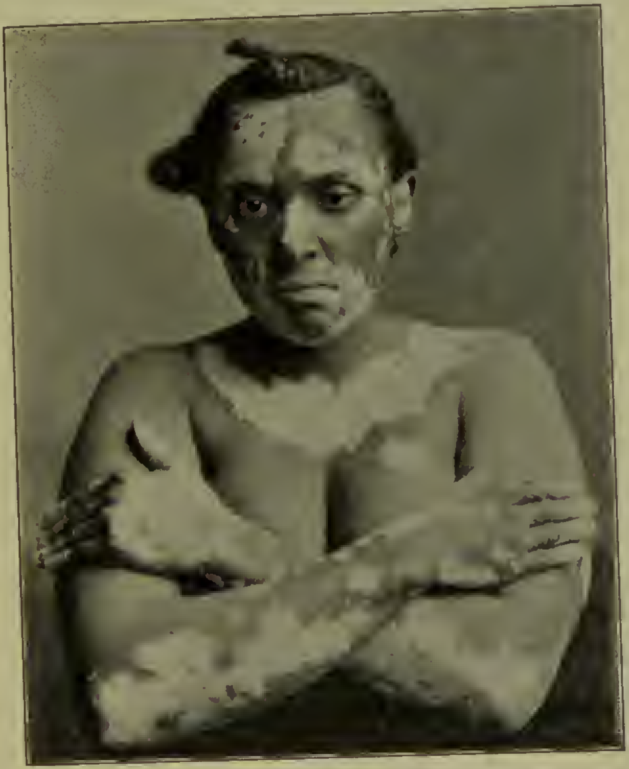

FIG. 285.—Vitiligo or leukoderma (Schamberg).

Atrophic conditions of the skin are also seen as a result of abdominal distention in pregnancy, ascites, neoplasms, etc., and in various nervous diseases.

Neurotrophic lesions of the skin in chronic diseases of the nervous system have been studied by Paget and S. Weir Mitchell. The skin becomes red, thin, shining—*glossy skin*. The subcutaneous tissue also wastes, so that the finger-tips become pointed. The growth of hair and nails is retarded, and the nails become brittle.

Secondary atrophies of the skin succeed such conditions as syphilis, tuberculosis, chronic inflammations, etc. *Kraurosis vulvæ* is an atrophic disease of the skin of the vulva with marked loss of tissue.

Necrosis of the skin is usually associated with diseases of the spinal cord and peripheral nerves, with loss of trophic innervation and the formation of *decubitus* or *bed-sores*. Infection commonly changes the necrosis to gangrene.

Gangrene of the skin invariably accompanies death of the extremities. Indeed, in senile gangrene and in other forms as well the gangrene begins in the skin and spreads to the deeper tissues. Gangrene affecting the skin alone is not infrequent in diabetes. Symmetric gangrene occurs in Raynaud's disease and some of the severe infections.

A peculiar form of disease of the skin and deeper tissues of the foot is called *malum perforans pedis*, or perforating ulcer of the foot, and consists in the formation of a rapidly and deeply spreading ulcer of the foot. The condition is in all probability neurotrophic, the lesion being gangrenous or necrotic. In some cases it may depend upon circulatory rather than upon nervous changes.

Gangrene of the skin may also follow the application of 5 per cent. carbolic acid for even a short time.

Hyperplasia, keratosis cutis, or cornification of the skin, may be excessive and lead to various forms of hyperplasia.

Callosities are local thickenings of the epidermis, usually observed upon the palms and soles, where the friction of working and walking is received. Somewhat similar congenital or acquired formations in infancy are sometimes described as *keratodermia.*

Clavus, or *corn,* is a similar thickening of the epidermis in which only a small area of the tissue is affected. The circumscribed limits of a clavus permit it to be pressed upon the subjacent papillary tissues, which may atrophy or be stimulated to inflame. Suppuration sometimes occurs.

Cornu cutaneum, or *horn,* is sometimes formed upon the skin, and may attain considerable dimensions. They may develop from normal skin or from cicatrices or atheromata. Horns also grow from the matrices of the nails, especially those of the great toes.

Verruca, or *warts,* are true papillomata of the skin. The *condyloma acuminatum* is an inflammatory formation usually observed upon the genital organs and about the anus. It depends upon the irritation of gonorrheal and other inflammatory discharges, or upon the decomposition of smegma. The growth consists of a considerable enlargement of the papillæ of the skin, which often branch or divide and are covered with a thickened epithelial layer. The warts are usually irregular in shape, according to the number, size, and shape of the papillæ. The papillæ are well supplied with blood vessels, and are infiltrated with round-cells. There may be more or less well-marked lymphangitis in the neighborhood of the warts, which are usually multiple, irregular in size and shape, soft, of a reddish color, and somewhat translucent.

Keratosis follicularis, Darier's disease, or **psorospermosis follicularis** is a rare disease of the skin usually observed in childhood. The cause is not known. It is characterized by a primary hyperkeratosis and parakeratosis involving the sebaceous and hair-follicles. The mouths of the follicles are dilated and packed with funnel-shaped masses of imperfectly cornified cells. The characteristic changes occur in the rete, which contain round bodies bearing a strong resemblance to parasites, and hence called *psorosperms.* They are now supposed to be forms of cellular degeneration. There are also numerous compressed, homogeneous, shrunken bodies, best seen at the bottom of the follicle plugs, called by Darier "*grains,*" and fissures or lacunæ between the rete cells, resulting from the pressure of the horny grains. The rete proliferates and thickens, and in places grows deeply into the corium, producing papilliferous areas. The stratum granulosum is absent from the lesions.

Elephantiasis Arabum is a most interesting affection, characterized by hyperplasia of the subcutaneous cellular tissue, which sometimes results in extreme deformity. The disease usually appears in the lower extremities or in the external genital organs. Elephantiasis of the leg is sometimes called "Barbadoes leg." The disease is of frequent occurrence in certain tropic and semitropic countries, especially Barbadoes, Arabia, Egypt, India, the Malayan Islands, and Central America. Sporadic cases occur in Europe and America. The darker races are more predisposed to it than is the Caucasian.

Manson has shown the disease to depend upon the Filaria sanguinis hominis. The disease begins as a febrile affection, sometimes as an afebrile hyperplasia of the connective tissues. Sometimes it seems to follow eczema and other chronic or frequently recurring skin inflammations.

The affected part assumes an enormous size, the leg sometimes becoming nearly as great in girth as the body; the scrotum has been observed to weigh as much as 100 pounds. The surface of the skin may be smooth, but upon the limbs is usually thrown into folds. The skin has a puffy, velvety appearance and is pale in color. The tissues may be soft and flabby when touched (*elephantiasis mollis*), or firm, hard, and white (*elephantiasis dura*).

Microscopically, the tissue beneath the skin is found to be enormously thickened and to consist of bundles of coarse fibers more regularly arranged than the normal areolar tissue. The blood vessels are dilated, and their walls thickened. The skin is usually thickened; it may be smooth or the surface may be marked by verrucosities or projections. When the epidermis is thickened and formed into coherent plates or scales, the affection is called *acquired ichthyosis* or *keratosis.*

Scleroderma is a form of induration of the skin caused by hyperplasia of the connective tissue and elastic fibers, and of the muscle-fibers of the corium. It is accompanied by narrowing of the lymph-spaces and lymph-vessels, with some cellular proliferation about the sweat-ducts, hair-follicles, and sebaceous glands, and in the adipose tissue. The upper layers of the corium may become so adherent to the fascia and periosteum, and the hyperplastic tissues may be so dense and hard that the hair-follicles, sebaceous glands, and sweat-glands may atrophy. There are no changes in the epidermis.

The disease may be diffuse (*sclerema*) or circumscribed (*morphea*). It is more frequent in women than in men, and usually occurs in neurotic individuals or in those with some disease of the nervous system.

The etiology of the affection is obscure. In some cases it is associated with changes in the thyroid gland. Sometimes it has succeeded repeated attacks of erysipelas and rheumatism. It has also been observed subsequent to exposure.

Sclerema Neonatorum.—This is a rare, usually fatal disease of the skin occurring in new-born infants and bearing some resemblance to scleroderma. It is chiefly seen in premature children or in those suffering from marasmus or other depressing conditions. Various explanations for the apparent "drying-up" of the skin are given. Some regard the process as infectious; Langer thinks it depends upon solidification of the fats.

Hypertrophy of the Skin.—**Ichthyosis** is a peculiar hypertrophic condition of the skin resulting from a remarkable tendency for the epithelial cells to transform themselves into the horny epidermis (*keratosis*). The disease may be congenital or acquired, and is usually general, though sometimes local.

All grades or degrees of the keratosis and hypertrophy present themselves, the mildest grade being known as *xerosis* or *xeroderma*, and consisting of little more than the minute, papule-like elevations about the hair-follicles caused by their mouths being filled with horny plugs, as seen in *keratosis pilaris.* The severest form consists in the immense thickening seen in *ichthyosis sauroderma*, or "crocodile skin."

Congenital ichthyosis is characterized by a markedly thickened, horny skin, sometimes folded and frequently interrupted by cracks or fissures of the superficial layers, so dividing it as to resemble alligator skin in very bad cases, and in mild cases to give the appearance of fish-scales. The hands and feet may be covered with dense, horny layers that interfere with proper development.

In the horny epidermis the lanugo hairs are caught and retained. The lower layers of the skin are usually atrophic, while the cells transform directly into horny cells without the intermediation of the granular layer. The pathologic changes are essentially hyperplasia and cornification of the epithelium.

Acquired ichthyosis usually begins with the occurrence of yellowish or brownish pigmented areas over which the horny layer of the epidermis thickens and becomes dry and shining. As the disease spreads, fissures and cracks occur, dividing the thickened epidermis into scales or plates.

The local forms of ichthyosis are characterized by thickening of the horny layers of the skin—*keratoma* or *ichthyotic warts*. The cause of the affection is entirely unknown.

INFLAMMATIONS OF THE SKIN.

Inflammation of the skin arises from many different causes and presents a great variety of appearances. Certain terms are used in describing the skin lesions that must be defined before they can be properly understood. Of these, the following are important:

Macule, or "spot," is any circumscribed, non-elevated, colored or discolored area upon the skin. Macules may be white when the normal pigment is absent, or may be brown or yellowish when an abnormal intensification of pigment occurs; they are pink, red purple, or blue when dependent upon hyperemia or hemorrhage of the skin. Old hemorrhagic spots may become greenish-yellow or yellow as the blood-pigment is absorbed. The red macules, when not large, are commonly spoken of as *roseola*.

Erythema is a diffuse redness extending over a considerable area of the skin. The color of an erythematous patch is nearly scarlet, thus differing very much from *lividity* or *cyanosis*, in which the color is bluish or ashen.

Papules are small, flattened, hemispheric or conic, solid elevations of the skin. They usually are about the size of a millet-seed or a pea, and are formed by a leukocytic infiltration of the skin occurring in the epithelial and papillary layers or sometimes in the corium.

Nodes or *tubercles* are larger prominences approaching a hazelnut in size. Very large nodes, as large as a walnut, are sometimes described as *phyma*.

Wheals are flat, tabular elevations, distinctly circumscribed, of rapid formation and disappearance, and probably dependent upon hyperemia and serous infiltration of the skin.

Vesicles are small prominences containing fluid. They have thin, transparent envelops composed of a few layers of the epidermis, and contain clear, serous fluid; or in less usual cases slightly bloody or slightly purulent fluid. Large fluid collections are usually formed by the union of vesicles, although they sometimes form independently and are known as *bullæ*.

Pustules are similar lesions which contain pus instead of serum. They are usually of a yellowish-white color, and are about the size of a millet-seed. *Achor* is a larger purulent collection, not usually very prominent, and perforated by a hair. Large pustules are called *ecthyma*.

Excoriations and *erosions* are lesions caused by loss of surface epithelium, by which an oozing of lymph and occasional injuries to the blood capillaries occur.

Ulcers are deeper destructive lesions than can be included under excoriations.

Fissures or *rhagades* are cracks in the tissue which may affect the epidermis only, or may descend through the entire thickness of the skin.

Crusts are dried masses of exudates and secretions collecting upon the surface.

Scales are masses of horny epithelial cells accumulated upon the upper layers of the skin.

Traumatic inflammation of the skin usually results from the action of extremes of heat and cold or from chemic agents. The result of the operation of the different causes is similar: thus in regard to burns it is possible to recognize certain degrees of damage done.

Burns of the first degree are characterized by erythema and swelling of the skin; *burns of the second degree*, by vesication and bulla formation; *burns of the third degree*, by destruction of all the layers of the skin and ulceration. Burns from carbolic acid and other caustic substances can frequently be similarly characterized. Chemic substances not infrequently modify the appearances by color or other characteristics peculiar to themselves; thus, burns from nitrate of silver become black; those from carbolic acid, white; and those from nitric acid, yellow.

Dermatitis venenata follows direct chemic or toxic irritation of the skin, and results from contact with numerous substances, such as poison-ivy, mustard, croton oil, and cantharides.

The use of bromin and iodin for medicaments may cause acneform inflammations of the skin, while belladonna, quinin, antipyrin, and some other drugs produce characteristic *dermatitis medicamentosa*.

Idiopathic Inflammations of the Skin.—Eczema.—Eczema is probably the most frequent and most varied inflammatory disease of the skin. It is an inflammatory affection of all the layers, characterized by multiform lesions, most frequently observed upon the face, hands, feet, and genital organs. Its appearance is more varied than that of any other disease. At times it is characterized by diffuse redness—*eczema rubrum* or *erythematosum*; at times by the formation of papules—*eczema papulosum*. If desquamation occurs, it may be called *eczema squamosum*. The formation of vesicles—*eczema vesiculosum*—is not at all infrequent, while the formation of pustules, probably from infections from the superficial layers of the skin, leads to the formation of *eczema pustulosum*. The lesions are dry or moist, according to the formation of vesicles and papules which rupture and discharge upon the surface. Very moist forms are sometimes called *eczema madidans*, and when the exudate dries upon the surface with the formation of considerable crusting, *eczema crustosum* occurs. From fissures and erosions of the skin some blood may escape and mix with the secretions.

Various secondary results of eczema occur, among which may be mentioned the formation of an excessive amount of epidermis, so that the skin becomes unduly horny. This condition has been described by Unna as *parakeratosis*. Rapid desquamation of the epidermis characterizes *eczema squamosum*.

The disease may be acute or chronic, the *chronic form* being more usually dry, and characterized by thickening of the corium and fibrosis of the subcutaneous tissue and deposits of pigment in the diseased areas. The *acute form* is subject to frequent relapses, and is apt to leave behind it a thickened, sometimes pigmented skin.

The histologic changes characteristic of eczema consist of inflammation of the corium, with consequent changes in the epithelium. There is always more or less hyperemia, with transudation of serum and infiltration of round-cells. The lymphatics are turgescent, and the cells of the corium proliferate. In mild cases only the papillæ and upper layers of the corium are involved, while in severe cases the inflammation may descend into the subcutaneous tissues, causing the lesions to resemble erysipelas. From collection of the inflammatory exudate and maceration of the cells vesicles and bullæ may form between the rete and granular or horny layers of the epidermis. Vesicles also occur in consequence of colliquative degeneration of the cells. The exudate from eczematous patches has a gummy character.

Associated with the active inflammatory processes one may also observe abnormalities in the cellular transformations, such as hypokeratosis, hyperkeratosis, excessive or deficient desquamation, etc.

Eczema folliculorum is not a true inflammation, and, therefore, not an eczema.

Eczema seborrhoicum occurs upon the scalp, especially of those who wear coverings all the time. In its mild form this affection has also been called *pityriasis capitis*. The derm usually shows mild inflammation with vacuolation of the rete, mitosis, and invasion by wandering cells. Severe grades more closely resemble ordinary eczema.

Dermatitis repens is a rare form of spreading inflammation of the skin starting from an injury. It is undoubtedly infectious.

Neurotic Inflammations of the Skin.—Of these, some have been mentioned, and do not require further description; for example, the *decubitus* of spinal disease, the *malum perforans pedis*, the necrotic and gangrenous lesions of Raynaud's disease. One of the peculiar dermal neuropathies is that known as *herpes zoster*, or "shingles," in which there is an acute formation of vesicles over the distribution of a nerve. The disease is unilateral, as a rule, and most commonly affects the skin of the thorax. The vesicles contain clear fluid, which in the course of three or four days becomes turbid and subsequently purulent and dry, with the formation of crusts. A theory recently suggested by Pfeiffer and Wasielewski is that the disease occurs in the distribution of a vessel, not a nerve, the capillaries being blocked by micro-organisms. In rare cases the herpes vesicles contain bloody fluid—*herpes zoster hæmorrhagica*.

The histologic changes in herpes zoster begin in the rete cells, which undergo rapid proliferation, some of them increasing greatly in size. Cavities are formed containing portions of the degenerated cells. Hartzell and others have described protozoa-like bodies in the cells.

The so-called *glossy skin* is looked upon by many as a chronic form of dermatitis.

Infectious dermatitis, as opposed to *exanthematous dermatitis,* to be described later, is a term including forms of inflammation limited to the skin and its subjacent tissue and not those that are accidental consequences of a general systemic infectious disease.

Herpes simplex (*herpes facialis; herpes labialis; herpes progenitalis*) is not infrequent, certain persons being apparently predisposed to it. The cause of herpes is not known. It may be infectious, but experience shows that it accompanies indigestion, cold, etc. It is particularly common in pneumonia. Progenital herpes may be due to lack of personal cleanliness, etc.

Simple dermal abscesses are not infrequent in consequence of spontaneous infection of the sweat, sebaceous glands, and hair-follicles, punctures and lacerations of the skin from accidental injuries and surgical sutures, etc. When in connection with hair-follicles, these little abscesses are often spoken of as *sycosis.* The lesion is an abscess, the cocci or other micro-organisms causing the trouble being, as a rule, readily demonstrable in the pus.

The etiologic elements—namely, the cocci—are probably usually derived from the skin itself, where they normally abound, though they may be carried in by needles, splinters, etc., from other sources.

Furuncles or **boils** are more extended suppurative lesions caused by a wider distribution of the cocci and the invasion of more tissue, the invasion beginning in a hair-follicle and its sebaceous glands. The lesion is usually of a purple color, projects from the surface, is the size of a pea, hazelnut, or walnut, and is very painful. In the process of suppuration the colliquation necrosis of the tissue leads to the formation of a central slough, which, when separated, forms the "core" of the boil. The lesion heals by evacuation and cicatrization.

Boils usually occur in young persons at situations where the skin is irritated or abraded by clothing, etc. The infection depends chiefly upon the Staphylococci albus and aureus.

Carbuncles (*benign anthrax*) are larger suppurative lesions of the skin, frequently situated upon the back of the neck, and occurring in persons beyond middle life. Diabetes and other systemic and constitutional depravities markedly predispose. The carbuncle is usually a large lesion, 3 to 8 cm. in diameter, which may be compared to an aggregation of small boils. It is elevated, purplish, firm, and very painful, and is frequently surrounded by an edematous zone. Carbuncle differs from furuncle in that the inflammation spreads in the subcutaneous tissue and from it extends upward along the fat columns, producing new foci of suppuration and necrosis of the overlying skin, by which numerous exits for the inflammatory products are formed. In the course of several days suppuration occurs at many points, and evacuation occurs through a number of superficial openings, so that the appearance was described by the older surgeons as similar to a "pepper-box."

The disease is apt to cause profound systemic intoxication, and is not rarely fatal. Its cause is not accurately determined. Bacteriologic examination usually shows the presence of streptococci and staphylococci.

Erysipelas is an acute inflammatory disease of the skin depending upon streptococcus infection. It may occur spontaneously, probably from inoculation of the micro-organism into minute, perhaps invisible, lesions of the skin in the neighborhood of the nose and mouth, or from the inoculation of wounds. The spontaneous form usually selects the face, and hence is often described as *facial erysipelas*. Whether spontaneous or traumatic, the disease is characterized by a rapid invasion and the formation of a flat, tabular elevation of a peculiar rosy-red or "erysipelatous" color, with a shining surface and a sharp demarcation from the surrounding tissue. The inflamed tissue is edematous, readily pitting upon pressure. Its surface is often occupied by vesicles, and the contents of the vesicles often become clouded and form pustules. There are much fever and profound systemic depression. There is rarely much pus-formation, and microscopic examination of the tissue shows the chief field of operation to be the lymphatic channels in which the streptococci multiply and spread. There is some round-cell infiltration. The disease recovers by absorption of the exudates, and it is unusual to have any extensive tissue destruction, though gangrene sometimes occurs.

Dermatitis Herpetiformis or Duhring's Disease (*Hydroa Herpetiformis; Dermatitis Multiformis; Herpes Gestationes; Pemphigus Pruriginosus, etc.*).—This is a peculiar disease, which Duhring classifies as midway between erythema multiforme and pemphigus. It consists of an acute inflammation of the papillary layer of the skin, the epidermis and deeper layers being scarcely affected. Edema is always present and often excessive, the papillæ are invaded by polymorphonuclear leukocytes and occasional erythrocytes, and often many eosinophilic cells are present. Vesicles form between the derm and rete. There is a slight perivascular cellular invasion of the cutis. The exudate is fibrinous, and at times the contents of the vesicles cloud and become slightly purulent.

The etiology of the disease is not understood. It occurs during pregnancy and in various conditions of depraved vitality, such as accompany renal and other organic affections. It is also sometimes observed in nervous debility.

Impetigo herpetiformis is also a very rare and usually fatal affection, characterized by superficial pustules which appear to be metastatic abscesses of the skin. A few writers consider the lesion to be the result of a neurosis.

Pemphigus is a disease of unknown etiology, characterized by the formation of large vesicles upon the skin. The vesicles vary in size from a pea to a goose-egg. The contents are at first clear, later becoming clouded and finally purulent. Eventually they coagulate or evacuate, crusts forming and the lesions healing, either readily and perfectly, or so slowly and imperfectly that the convalescence is delayed for months or years. The disease may be fatal. The acute contagious pemphigus of the new-born and some of the pemphigoid affections of the tropics are probably different affections of microbic origin.

Pemphigus is divided into *acute pemphigus* or *dermatitis bullosa* and *chronic pemphigus*. The acute form usually lasts one or two weeks and recovers readily, being closely related to the acute infectious diseases in its course. The chronic form is divided into the common (*pemphigus vulgaris*), exfoliative (*pemphigus exfoliativa*), and vegetative (*pemphigus vegetans*) forms.

1. *Pemphigus chronicus vulgaris* resembles the acute form, but is of longer duration.
2. *Pemphigus chronicus foliaceus* is a form in which, without the previous formation of blebs, there are local loosenings and exfoliations of epidermis, leaving moist surfaces which become covered with crusts and slowly heal. This form lasts for months and years and may be fatal.
3. *Pemphigus chronicus vegetans* is a form in which the lesion is situated upon the tender skin of the genitals, groins, axillæ, or in the mouth, vagina, pharynx, larynx, etc., and is characterized by the occurrence of the bleb, the separation of its epithelial covering, and the subsequent formation of warty and papillary outgrowths from the denuded surface.

When the lesions of pemphigus are studied microscopically, it is found that the entire epidermis is affected and is elevated from the cutis, which is secondarily degenerated, exhibiting colliquation of the cells and degeneration of both collagenous and elastic tissues. Later, in the stage of cloudy exudate, it is found that leukocytic infiltration has occurred. The fluid of the blebs is in part the result of colliquation of the cells, in part of inflammatory exudation. In the form known as *pemphigus hæmorrhagicus* it is stained by blood.

The cause of pemphigus is still uncertain, though various observers have claimed the discovery of micro-organisms specific for the affection and capable of reproducing it in animals.

Herpes is probably an infectious disease of the skin which often occurs spontaneously, though very frequently during the course of other affections, especially pneumonia, typhoid fever, and malaria.

The lesions consist of groups of vesicles containing clear serous fluid which in the course of time becomes turbid. These lesions persist for a few days, then dry, crust, and heal. They frequently occur in crops.

Various forms are described: *Herpes zoster*, already mentioned, occurs in the distribution of certain nerves and may be of nervous or arterial origin. *Herpes facialis* or *labialis* is common upon the lips and face. This condition, when mild, is known to every one as the "fever-blister." *Herpes præputialis* occurs upon the penis, clitoris, labia, etc.

Lichen planus is a peculiar, papular skin affection occasionally observed in persons of neurotic temperament, supposedly resulting from disturbances of innervation. Torök describes the lesions as depending upon an inflammation of the upper layers of the corium, with secondary changes in the epidermis. The papillæ and a narrow, sharply outlined zone of tissue beneath them are infiltrated with cells like leukocytes, and are more or less edematous. The rete cells undergo proliferation, which in chronic cases may be so excessive as to obliterate the papillæ, or, on the contrary, to enlarge them by downward growth of the interpapillary processes. These cells of the rete are not so conspicuous in the acute cases, and instead of undergoing hyperplasia, may become atrophied by crowding of the infiltrating cells from below. The stratum corneum being thickened, conic masses of horny epithelial cells form about the orifices of the sweat-glands, leaving a central depression in the papule when exfoliated. Some observers think vesicles form between the rete and papillæ at one stage of the affection, and regard the umbilication of the papules as depending upon the absorption of the contents of the vesicles.

The etiology of the disease is not understood.

Anthrax, or **malignant pustule,** is, fortunately, a rare affection of the skin following infection by the Bacillus anthracis. It usually occurs in those whose occupations bring them into contact with the flesh, hides, hair, or other parts of diseased animals, from which the specific infection is derived. The infection may take place through any small lesion, and has been known to follow the bites of insects which have preyed upon infected materials or animals. The disease usually manifests itself upon the face, neck, hands, and shoulders, beginning with the formation of a small red papule resembling a flea-bite, surrounded in from twelve to fifteen hours by a small vesicle containing brownish or bluish fluid. When not scratched, the vesicle dries and forms a scab. The surrounding skin is somewhat reddened, indurated, and swollen. The affected area enlarges in depth and width, the color darkens, and finally a black eschar is formed. This is at first superficial, but gradually involves the deeper layers of the skin. The black spot varies in size from 2 mm. to 2 cm.; it is hard and dry on the surface, and there is no indication of suppuration. Subsequently a new set of vesicles forms about the eschar, giving it the appearance of a ring set with pearls. In some cases it has an appearance not unlike a vaccine vesicle. The vesicles coalesce, and their contents may be somewhat discolored by blood. The surrounding skin may become reddened and swell considerably, so as to form a distinct tumor—*carbuncular tumor*. If the disease continues to spread, the swelling may become great and very extensive. Fresh crops of vesicles often appear. The progress of the disease takes from three to nine days, when a line of demarcation forms around the eschar and the slough separates, leaving a cicatrizing surface which heals without suppuration.

The disease is characterized by Raimbert as without pain, without pus in the initial lesion, and with the formation of a vesicular areola, not purulent and of limited dimensions.

Not infrequently the disease becomes erysipelatous in character and suppuration and gangrene may occur. The systemic complications are profound in most cases, and the infection is commonly fatal. When the lesions are examined bacteriologically, the specific bacilli are usually readily detected. They have also been secured from the blood before death. When not found in the original lesion, they may be found in other parts of the body. The local infection is complicated by the presence of putrefactive bacteria, which at times seem able to destroy the anthrax bacilli, and it is not impossible that some cases recover through these means.

The histology of the lesions consists of an acute inflammation with much edema, a serofibrinous exudation, and more or less necrosis. Bacilli are easily defined in the cells, between the cells, and in the lymph-spaces.

Impetigo, formerly differentiated as *impetigo simplex* and *impetigo contagiosum*, is a pustular disease of the skin which depends upon infection with pus cocci. It occurs in badly nourished children. The pustules are situated in the derm only, and are not destructive in tendency, healing without scars.

Ecthyma is a more intense degree of the same process, the pustules being larger, deeper, and more destructive. The lesions may be succeeded by pigmentation.

Chancroids are infectious lesions of the skin and adjacent mucous membranes of the genital organs, usually resulting from inoculation during coitus. The lesion is observed about twenty-four hours after infection, and begins as a vesicle or pustule which rapidly forms a destructive ulcer with a yellowish, purulent base, irregular infiltrated edges, soft consistence, and a marked tendency to spread. There is apt to be rapid lymphatic extension to the inguinal glands, which usually also suppurate. A small bacillus described by Ducrey is supposed to be the cause of the disease.

Tuberculosis of the skin may be primary or secondary. The secondary forms occur as small, superficial, rounded ulcers, usually about the mouth, genitals, or anus; or in the forms known to the older writers as *scrofuloderma*, consisting of small, rounded, isolated nodules in the subcutaneous tissues, which soften and form ulcers with indurated edges. The lesion first described probably results from direct implantation of the bacilli from infected discharges; the second probably sometimes from hematogenous distribution of the bacilli, sometimes from direct implantation of the bacilli in the skin. By far the most frequent forms of tuberculosis of the skin are *lupus* and *verruca tuberculosa*.

Lupus erythematosus is a form of primary tuberculosis of the skin characterized by the formation of slightly elevated red patches, usually upon the nose, lips, or cheeks. From the surface of the patches the epidermis becomes loosened and desquamates. Slight pressure often suffices to rupture the covering of the subepithelial tubercles and allow the escape of their contents, after which shallow, slowly but persistently increasing ulcers form; as these spread at the periphery the center usually slowly cicatrizes.

Lupus vulgaris differs in that without any inflammatory hyperemia the formation of tubercles takes place in the cutis and elevates the skin so that papules are formed. The disease usually begins upon the face, but the limbs and trunk are not infrequently affected.

The lesions are very polymorphic in consequence of what are really slight variations in the pathologic process. The affection usually begins in a single little papule caused by the formation of granulation tissue inclosing true tubercles. The coagulation necrosis of the tuberculous tissue soon causes rupture of the suprajacent epidermis and the formation of an ulcer, which, after the evacuation of its contents, may heal, or, in less favorable cases, may continue to spread. The eruption, rupture, and cicatrization of the tubercles form the most favorable course the disease can run, though this is in itself disfiguring, from the formation of a larger or smaller area of skin rich in granulation tissue, studded with new tuberculous papules, and seamed by cicatrices. The formation of spreading ulcers is much more destructive, and consequently extremely disfiguring, and leads to *lupus exulcerans.* When the loss of epithelium is marked, the condition is called *lupus exfoliaceus.* The scar tissue is sometimes excessive, sometimes hypertrophic, and produces indurations, warty outgrowths, polypoid excrescences, ridges, seams, stellate cicatrices, etc. This causes the occurrence of *lupus verrucosa, papillaris, tuberosa, nodosa, hypertrophica,* etc., according to the appearance presented. The irregularities of arrangement in lupus, together with the frequent infections and the possible entrance of the "cancer parasite," are sometimes the cause of epitheliomatous changes, which may progress more rapidly than the original disease and completely mask it.

A not uncommon limited form of dermal tuberculosis is that known as *verruca tuberculosa,* or *anatomic tubercle.* The lesion is seen upon the hands of anatomists, surgeons, pathologists, veterinary surgeons, servants in anatomic and pathologic laboratories, and butchers. It results from the direct tuberculous inoculation by needle-pricks, knife-punctures, etc. The lesion is a papillary hypertrophy with epidermal hyperplasia and desquamation. Macroscopically it usually appears as a purplish, elevated, rough, papular area. Microscopically tubercles are found in the rete and in the subepithelial layers. There are usually very few tubercle bacilli present.

In general miliary tuberculosis Leichtenstern has observed small red papules upon the skin, which resulted from the formation of small dermal tubercles.

The tubercles found in cutaneous tuberculosis do not differ in histology from those of other parts of the body. The number of bacilli in the lesions is usually extremely small.

Syphilis is a disease with numerous manifestations upon the skin. Some of the lesions are highly characteristic; others are recognized with much difficulty.

The *chancre,* or primary lesion, is occasionally seen upon the skin of the genital organs from contact during coitus, and is sometimes also seen in consequence of direct implantation, as in tattooing, etc. The cutaneous chancre is not very characteristic in appearance. It may present itself—(*a*) As an indurated papule, parchment-like superficial induration, or a split-pea-like subepithelial induration, which may heal in the course of a few weeks without attracting any attention. (*b*) As an induration, which, after a time, suffers desquamation of the epithelium, necrosis of the upper layers of the corium, the formation of an erosion, and sometimes of an ulcer. Such an ulcer may be characterized by sufficient induration to make its nature clear, or may become infected quite early with accidentally present cocci, etc., and become inflamed, hyperemic, soft, and devoid of its essential characters. (*c*) Rarely the chancre begins as a vesicle which speedily becomes an ulcer by loss of the epithelium. Microscopically the lesion presents the cellular infiltration and vascular changes described in the section upon Syphilis.

The eruptions of *constitutional syphilis*, depending upon the generalization of the poison through the blood, are extremely varied. They may be common to the entire body, or limited to the buttocks, back, trunk, etc. When widely distributed, they differ from other similar eruptions in the frequency with which they occur upon the palms of the hands and soles of the feet. They have, as a rule, a peculiar copper-red color and a tendency to a rounded form. All the essential forms of exanthema may occur. The affection may take the form of macules, papules, pustules, ulcers, blebs, or gummata. The affection may be very slight, or so severe as to threaten life, if not in some cases to cause death.

By dermatologists the lesions are named from their resemblances to simple skin affections, thus: *Roseola syphilitica*, *lichen syphiliticus*, *pemphigus syphiliticus*, *impetigo syphilitica*, *psoriasis palmaris syphilitica*, etc.

The most frequent and most important skin lesions are the *chancre*, the *roseola*, the *condyloma latum*, the *rupia* (large pustular syphiloderm), and the *gumma*. (For descriptions of the histology of these lesions the student is referred to the chapter upon Syphilis in Part I.) They are all essentially characterized by round-cell infiltrations with a marked tendency to localize about the blood vessels, which are always turgescent in and about the lesions.

The syphilitic skin affections may heal kindly, leaving no marks behind them, or may cause white or pigmented areas which remain for a time; or, as is most frequent, cause scars which slowly undergo cicatricial contraction. Very little permanent disfigurement results in the ordinary case of dermal syphilis.

Lepra of the skin may be either tubercular—*lepra græcorum*—or anesthetic—*lepra anæsthetica*. Description of the lesions is given in the section upon Leprosy.

Glanders.—The skin lesions of glanders usually appear as papules, nodules, vesicles, bullæ, variola-like pustules, or as phlegmonous or erysipelatous inflammations. Deep sloughing ulcers and even gangrenous patches may be observed. The lymphatic vessels and glands enlarge, to form the *farcy buds*, and subsequently ulcerate. The disease not being peculiar to the skin, and readily extending from it to other tissues, merits no further mention here.

Rhinoscleroma and **mycosis fungoides** have been described at some length in Part I.

Toxic Inflammations of the Skin.—*I. Inflammations of the Skin Caused by Contact with Irritating Substances.*—Some local irritants, such as poison-ivy, cantharides, mustard, croton oil, carbolic acid, sulphuric acid, etc., cause traumatic injuries of the skin, even reaching the point of gangrene.

Ivy-poisoning.—Contact with the leaves of *Rhus toxicondendron* or *Rhus radicans* affects the skin of susceptible individuals very markedly, producing an erythema, with vesication, oozing, crusting, and a marked tendency to spread from place to place, so that some have thought the serum from the vesicles contained the irritating substance.

Cantharides, mustard, and the stronger water of ammonia, when applied to the skin, produce erythema and vesication. Prolonged application may be followed by sloughing.

Croton oil differs from most local irritants in that its application is followed by the formation of large numbers of small pustules.

II. Inflammations of the Skin Depending upon Irritative Substances Circulating in the Blood.—Irritants circulating in the blood sometimes cause skin lesions, some of which are mild, some severe.

Among those best known is *urticaria*, which sometimes occurs after eating certain foods, such as strawberries, shell-fish, cheese, etc.; *erythema* and *roseola*, rarely papules, vesicles, and petechiæ, result from similar causes and after the administration of such drugs as atropin, quinin, morphin, strychnin, digitalis, salicylates, phenacetin, antipyrin, sulphonal, calomel, etc.

Doubtless the retained excrementitious products of faulty digestion and incomplete metabolism play an important rôle in the production of skin eruptions or in paving the way for local skin infections. Thus, in albuminuria and diabetes local gangrenous patches of the skin are frequently observed, and diabetes is a common predisposing cause of boils and carbuncles.

Urticaria is an angioneurotic affection of the skin usually resulting from intoxication. Very different causes may induce it, and it may result from external or internal stimuli. Mechanical, thermal, and chemic irritations of the skin, poisons absorbed from the alimentary system, psychic conditions, such as profound emotion and individual idiosyncrasy, may all have important bearings upon its etiology. In certain nervous affections a most marked predisposition to urticaria occurs in the form of *dermatographia*, in which drawing a pencil or other bluntly pointed instrument over the skin causes a corresponding urticarial elevation to follow in a few moments.

It is supposed that the wheals depend upon spasmodic contraction of the vessels, followed by their subsequent paralytic dilatation and the formation of an exudation which rapidly accumulates and is later rapidly absorbed. The redness of the wheal at first depends upon the hyperemia, while the subsequent central pallor is caused by the exudate expressing the blood from the capillaries. In *urticaria factitia* Gilchrist observed all the phenomena of inflammation within fifteen minutes after its formation.

In rare cases the urticaria, if severe, may be followed by vesication, and in still rarer cases the vesicles may contain blood-stained fluid. These recover with the formation of pigmented patches (*urticaria pigmentosa*). Unna and Gilchrist believe that the pigmentation is not so much dependent upon the hemorrhage into the cutis as upon the presence of accumulated pigment in the lower layer of the rete.

Prurigo, a papular disease of badly nourished infants, is thought by some to result from urticaria. It is a poorly characterized affection, of which the chief feature seems to be the formation of permanent papules. In some of them Leloir has observed a cystic degeneration of the cells of the rete.

The exanthematous diseases are characterized by skin eruptions due in part to the local action of the specific cause of the disease, in part to its toxic products, and in part to the faulty elimination of excrementitious products. Our knowledge of the diseases is too limited to permit of an accurate classification.

Scarlatina is characterized by a bright red, occasionally livid, slightly swollen condition of the skin. It usually begins upon the neck and clavicular regions, the groin, under the arms, on the loins, the back, the breast, the face, and the extremities, in irregular patches which later coalesce. Not infrequently small dark points are scattered over the reddened surface. This condition persists for about a week, sometimes only one or two days, and then gives way to a slightly yellow-brown pigmentation. The process terminates in desquamation, which may be very slight and furfuraceous, or may be so extensive that large areas of the epidermis peel off intact. This is especially noticeable upon the fingers and toes, which sometimes shed the epidermis like a glove (*desquamatio membranacea*). Rarely the eruption is marked by a papillary, vesicular, bullous, or hemorrhagic tendency.

The disease is characterized microscopically by a decided hyperemia, a slight degree of cellular infiltration, and a collection of exudate in the stratum granulosum, with colliquation of its cells and subsequent desquamation of the outer layers. There are very few changes in the papillary layer of the skin.

Mallory has recently discovered what appear to be protozoan parasites in the epithelial cells, but the true nature of the bodies described and their relation to scarlatina remain to be proved.

Measles is characterized by a pinkish, maculopapular eruption, which in exceptional cases becomes hemorrhagic (*black measles*). It appears first upon the face and neck, then upon the delicate parts of the skin of the trunk. The eruption consists of very slightly elevated, rounded spots, which run together irregularly to form larger patches of a somewhat crescentic shape. The skin is always mottled and spotted, the eruption never becoming confluent. There is always some hyperemic swelling, especially of the face, which appears bloated. The eruption lasts but a few hours, then begins to fade, is followed by a yellowish pigmentation, marked dryness, and a powdery desquamation.

The microscopic changes consist of hyperemia, transmigration of a few leukocytes, swelling, then drying and desquamation of the superficial layer of epidermis.

Typhoid fever is characterized by an eruption of rounded or oval rosy spots of pin-head or pea size, appearing in successive crops upon the abdomen and chest, sometimes upon the back, thighs, and arms, rarely over the entire body. The spots are usually few in number. They are rosy red, not elevated, readily disappear upon pressure, and never become petechial. They seem to consist of small subcutaneous or cutaneous hyperemias, and are probably dependent upon the presence of typhoid bacilli, as these have occasionally been cultivated from blood drawn from them.

In addition to the roseola, *sudamina* or *miliaria* not infrequently occur in typhoid. Sudamina are small vesicles which appear to depend upon elevation of the superficial layers of the epidermis by the pressure of the secretions of sweat-glands whose orifices have been occluded. They are probably not inflammatory in origin.

Typhus fever has a characteristic skin eruption which is described as consisting of several distinct elements. There is, first of all, an ill-defined subcuticular mottling of a dusky-red color, seemingly deep down in the skin; second, a widely distributed series of small, rounded red spots which at first disappear upon pressure, but later become petechial. The eruption may be copious, is sometimes mistaken for measles, but is more apt to be petechial. It persists after death. It usually appears first upon the face.

Varicella is characterized by the early appearance of red blotches and papules, upon each of which a little vesicle forms after a few hours. The vesicles are usually not umbilicated, and are small, but may be distinctly umbilicated and very large. Those not destroyed by scratching dry up in a few hours, forming small crusts. Before drying the vesicles may become filled with turbid fluid. Actual pustules are unusual. Scars are not infrequent after the larger lesions. Rarely the lesions may be of enormous size and suggest ecthyma. The vesicle formation is supposed by Unna to depend upon colliquation of the cells. Peculiar multinuclear cells found in the vesicles have been regarded by some writers as parasites, but Gilchrist has apparently shown this to be an error.

Variola is characterized by the most marked and interesting of the exanthematous lesions. The appearance of the eruption is usually preceded by red blushes of the skin much resembling scarlatina, but in some cases simulating measles.

The eruption itself begins with the formation of pin-head-sized hard and firm papules which have a faint red color. Each is usually surrounded by a hyperemic zone. By the fifth or sixth day from the beginning of the disease the papules begin to change into vesicles containing clear, amber-colored fluid, and each typical vesicle is distinctly umbilicated at the center. In rare cases hemorrhage occurs into the vesicles. In ordinary cases, by the eighth or ninth day the vesicles begin to change into pustules and the central umbilication disappears, the lesions becoming more globular in form and the color grayish-yellow. The pustules are usually surrounded by an injected, swollen zone. By the eleventh or twelfth day the pustules dry, or in bad cases rupture, and crusts form, dry, and desquamate, leaving pits which remain permanently if the papillary layers of the skin have been affected.

This course is typical of the discrete form, the confluent form being characterized by so many lesions that the pustules coalesce, while the hemorrhagic form presents many variations.

In the usual discrete form the eruption begins, as a rule, upon the forehead and wrists. In the confluent form the pustules are far more numerous upon the face and hands than upon the body and limbs. In these cases the rupture of the pustules converts the entire face into a suppurating surface, so that the patient presents a most revolting and pitiful appearance. In such cases the papillary layer of the skin is sure to be destroyed, and cicatrization with scar formation occurs. It may be some weeks before the cicatrization is completed, and the scars, which are at first red and conspicuous, do not whiten for months.

The hemorrhagic small-pox or *black small-pox* is characterized by the occurrence of hemorrhage into the pustules. "The skin may have a uniformly purplish hue, and the unfortunate victim may even look plum-colored. The face is swollen, and large conjunctival hemorrhages with the deeply sunken cornea give a ghastly appearance to the features." The hemorrhagic form of the disease is usually fatal.

The microscopic changes of the skin in small-pox consist in a primary circumscribed hyperemia of the papillæ and exudation into the rete. The cells of the rete become swollen and undergo coagulation necrosis just above the papillæ. The cells swell and gradually form anuclear, pale granules. This swelling and degeneration are succeeded by an inflammatory transudation in which many of the epithelial cells dissolve, forming the vesicle, which appears under the microscope as a cavity occupied by threads and flakes consisting of epithelial remnants, leukocytes, and fibrin. The umbilication seems to depend chiefly upon the presence of the original coagulation necrotic mass, which, not dissolving so readily as the neighboring cells, holds down the epidermis. The depth to which the vesicle descends varies, but it rarely involves the papillæ. The tissue immediately surrounding the vesicle is hyperemic and infiltrated with leukocytes. This is especially true of the papillæ. From the surrounding tissue the leukocytes invade the vesicle, which then becomes a pustule. As the leukocytes begin their active emigration the trabeculæ within the vesicle and the central degenerated mass melt away, the umbilication disappears, and the collection of pus becomes spheric. The crusts form by the drying of the exudate. As the activity of the process subsides, the leukocytes wander back into the lymphatics, and the swelling of the skin disappears. When the severity of the pustule formation causes destruction of the papillary layer, cicatrization and scar formation are inevitable.

The epithelial cells show in their nuclei and cytoplasm small spheric bodies supposed by many to be the specific parasites. This is, however, not yet proved to be the case, and there is as yet no definite information regarding the etiology of the disease.

Vaccinia, whether variola modified by passage through the cow or an independent disease, is characterized by the formation of a lesion at the point of inoculation, and sometimes elsewhere, which goes through about the same cycle of changes as characterizes the lesions of variola. It is first a papule, then a vesicle, next a pustule, and finally a scab, under which cicatrization occurs. The morbid anatomy and microscopy are identical with variola, and supposedly similar parasitic organisms are found in the lesions.

Fungous Diseases of the Skin.—These parasitic affections are caused by vegetable organisms of higher type than those already described, and are hence given a separate class. The fungi are in part related to the molds, in part to the yeasts, while others are not yet satisfactorily placed.

Favus.—Favus is a mycotic, inflammatory disease of the skin caused by the *Achorion Schönleinii*, and characterized by certain peculiar sulphur-yellow concave incrustations known as *favus cups*. The disease is not uncommon among the lower animals, and is perhaps originally contracted from them, though it is readily transmitted from man to man.

The disease usually occurs upon the scalp or face, though it may occur elsewhere upon the body. Infection seems to occur chiefly through the hair-follicles. The fungus grows between the layers of horny epithelium, forcing them apart and tending to elevate them. The center of the invaded area is probably held down by the hair, while the edges are raised, the "cup" being thus formed. The fungus readily invades the hair-follicle and the inner root-sheath, usually in the upper three-fourths of the follicle, though sometimes extending for a considerable distance into the hair itself. The fungus is easily recognized by its size, its long, occasionally branched, mycelial threads, with numerous transverse septa, and its many spores, which, somewhat irregular in size and shape, are chiefly situated at the ends of the threads.

The disease occasionally affects the roots of the nails, growing between the horny layers. The fungus may in time cause atrophy of the nail papillæ as well as of the hair-follicles, and eventually lead to alopecia and deformity of the nails.

Ringworm, a mycotic inflammatory disease of the skin, is caused by several parasites which invade the hairs and hair-follicles. Two chief forms of parasites are described—one with minute spores, called the *microsporon*, the other with large spores, the *megalosporon* or *trichophyton*. All forms of ringworm are contagious, and are probably originally derived from the lower animals, among which they are common.

The *microsporon* is characterized by mycelia, which form only in the hairs themselves, and, after dividing and subdividing, finally terminate on the outer side of the shaft of the hair in fine filaments upon the ends of which multitudes of spores are massed. The greatest massing of the spores is observed about the outer surface of the follicular portion of the hair.

The *trichophyton* rarely shows any mycelia in the lesions or in the invaded hairs, but appears in the form of parallel rows of spores within and upon the surface of the hairs.

The seat and peculiarities of the lesions govern the names applied to them. Thus:

Tinea circinata is ringworm of the hairless portions of the body. It makes its appearance especially where the skin is warm and moist. The fungus usually observed is the trichophyton, which grows in the deeper layers of the horny layer of the skin and sometimes among the epithelial cells down to the rete. In this form the mycelia of the trichophyton are present and spread centrifugally, forming the rounded or circinate lesions. The reaction consists of a mild inflammation characterized by hyperemia. A few papules form about the edges of the reddish patch.

Tinea tonsurans, or ringworm of the scalp, is frequent in children and more rare in adults. It usually depends upon the microsporon, which grows in the hair-follicle and in the hair itself, producing deformity and brittleness of the hairs. In consequence the hairs break off near the scalp, the broken ends having a frayed-out appearance. Centrifugal growth is the rule, resulting in a rounded area of very short hair upon a mildly inflamed base.

Tinea sycosis, or "barber's itch," is very similar to tinea tonsurans, except that it affects the beard of adults. It is caused by the trichophyton. It is a more inflammatory affection than ringworm of the scalp, and seems to depend upon follicular infection. There is considerable follicular inflammation, and the hairs may loosen and come out. The small abscesses of the sebaceous glands and hair-follicles may depend more upon secondary infection than upon the trichophyton itself.

Tinea imbricata occurs in tropic countries, and is caused by a fungus resembling the trichophyton, though it grows only in the epidermis and does not infect the hair-follicles.

Tinea versicolor, sometimes called *pityriasis versicolor*, is due to a fungus known as the *Microsporon furfur*. It occurs upon the hairless portions of the body, where the fungus grows between the upper layers of the horny tissue of the skin, producing a peculiar, yellow-brown color over irregular patches, with furfuraceous desquamation, but without inflammation. There is no involvement of the hair-follicles.

Erythrasma is a mycotic disease of the moist warm parts of the body where opposed surfaces come together, as in the axilla or groins. It is a very chronic disorder, and is thought to be due to a fungus known as the *Microsporon minutissimum*, of which the spores and threads are only about one-third the size of the *Microsporon audouini*. It is not yet proved that this fungus is specific. The disease is characterized by a slight redness and furfuraceous scaling, and has fairly well-defined edges, appearing to extend centrifugally.

Blastomycetic Dermatitis.—This is a chronic inflammatory and hyperplastic disease of the skin, caused by organisms closely related to the yeasts. The typical appearance of the lesion differs but little from verrucose tuberculosis, for which it is commonly mistaken, though it occasionally closely resembles epithelioma, for which it may also be mistaken. The areas of skin affected may be extensive, and are usually multiple, occurring in different parts of the body. The first appearance of the affection may be the formation of a papule or pustule which spreads slowly. Months or even years may be required in order that the lesions shall attain any considerable size. Larger lesions are irregular in outline, and show a dull, dusky, hyperemic base, upon which are crusted ulcerations, with thickened cicatricial areas and irregular thickenings of the epithelium. Montgomery describes a case in which the affection occurred upon the lower lip and could easily be mistaken for epithelioma.

Histologic examination of the lesions reveals interesting changes in both the epiderm and cutis. There is marked hyperplasia of the rete, the interpapillary processes of which descend somewhat irregularly into the corium, branching out much as in epithelioma. Signs of inflammatory disturbances are shown by the invasion of the epithelium by leukocytes, and occasional puriform clusters in the epithelium. Montgomery considers these little abscesses as characteristic of the affection. The rete cells are usually swollen, the prickles are very distinct, and the spaces between the cells are increased. Epithelial pearls are not infrequent as the result of irregular cornification.

The chief changes in the corium are the formation of small, inflammatory, cellular collections, some of which resemble abscesses, some tubercles. Giant-cells similar to those of tubercle are of frequent occurrence in the inflammatory collections, which are also characterized by polymorphonuclear leukocytes, plasma cells, lymphocytes, endothelial cells, and occasional mast-cells.

The *parasite* supposed to be specific for the affection is found in most of the inflammatory lesions, especially in the giant-cells. They appear as round, clearly defined, double-walled, homogeneous bodies, which commonly occur in pairs of unequal size. They measure from 7.5 to 20 μ in diameter. They require no special staining to define them, but can be seen in sections ordinarily stained with hematoxylon and eosin, though better in specimens prepared with methylene-blue.

The organism has been cultivated in a number of cases, growing upon some of the usual laboratory media, though rather better in beer-wort. Usually no fermentation has been observed. The multiplication by budding and the development of the spheroidal organisms into elongate hyphæ have pretty well established the yeast nature of the parasite.

Molluscum contagiosum, or **epithelioma contagiosum**, appears to be a parasitic disease of the skin, though it is uncertain whether the bodies heretofore described as parasites are coccidia or simply degenerated cells.

The disease consists of a tumor-like formation composed of a group of pea-sized or bean-sized, waxy-looking, shining nodules, surrounding a central, saucer-shaped opening.

Histologically the growth consists of a gland-like epithelial tissue, developing from the epidermis and inclosing large numbers of the supposed parasites. Each lesion is made up of a number of conic lobes separated by fibrous partitions and converging toward the central opening. The growth occurs entirely in the rete. The papillæ are obliterated by pressure or elongated to form the fibrous septa. Montgomery says: "The lower and outer cells of each lobule are usually normal, and correspond to the palisade cells of the rete, with which, at the border of the growth, they are continuous. Above them are cuboidal epithelial cells which undergo gradual degeneration toward the center of the growth, where they form a soft, homogeneous, yellowish mass, which can be pressed out through the central opening. The more minute changes, as well as their nature, are matters of dispute. By some the cell is said to undergo a homogeneous amyloid degeneration, the substance thus formed gradually filling up the entire cell, enlarging it, obliterating its structure, and forming the so-called molluscum body. The majority of observers describe the formation of clear oval spaces or bodies in the cell, beginning in the neighborhood of the cell-nucleus. These oval bodies are themselves provided with a nucleus, and gradually extend to fill up the whole interior of the cell. In its later stages the body is seen as a finely granular mass surrounded by a clear, transparent zone. Still later the exterior of the cell may undergo excessive cornification, a feature which constitutes the chief change in the cells. By a few observers these cell-forms found in molluscum are still believed to be protozoa, but the majority think with Gilchrist and Zuznitzski that they are changed epithelial cells."

The evident contagiousness of molluscum is strongly in favor of the parasitic nature of the contained bodies.

Erythema multiforme is a non-specific, inflammatory disease of the skin, resulting from the activity of various bacteria or their products, and characterized by reddish macules, papules, and vesicles. It occurs in association with rheumatism, syphilis, gonorrhea, and other bacterial affections, and not infrequently accompanies endocarditis, pericarditis, acute nephritis, and other disorders in which bacteria gain entrance into the blood. It also occurs in debilitated conditions arising from anemia, cachexia, chlorosis, etc., and at times appears as a result of various intoxications.

The pathology of the lesion appears simple. There is marked hyperemia of the corium and papillary layer, sometimes of the subcutaneous tissues, with an exudation between the rete and upper layers of the epiderm and the occasional formation of vesicles and bullæ. There is some hemorrhagic extravasation into the exudate, so that the tissue becomes pigmented, the pigment remaining after the disease recovers. Some leukocytes always invade the epiderm, and leukocytes are present in the fluid exudate of the vesicles and bullæ.

According to the extent of the damage done by the exudation and the type of lesion resulting, the disease can be divided into forms such as *herpetic* (*herpes circinatus*, *herpes iris*, etc.), *bullous*, *vesicular*, and *nodose*.

Erythema nodosum affects both skin and subcutaneous tissue, and is characterized by the formation of hyperemic swellings which may become as large as hen's eggs. Such lesions occur not only in the superficial tissues, but also occasionally in the muscles.

Dermatitis exfoliativa, sometimes called *pityriasis rubra,* is characterized by a universal inflammation of the skin with exfoliation of the epidermis. It may arise spontaneously or succeed other forms of dermatitis, such as eczema, psoriasis, etc. The etiology is unknown.

The histologic changes consist of a superficial inflammation of the corium, with vascular dilatation, edema, and round-cell infiltration, swelling of the papillæ with thinning of the rete, and exfoliation of the upper two-thirds of the horny layer. When the disease is chronic, the changes extend more deeply, connective-tissue hyperplasia occurs in the corium, and the cells of the rete become proliferated. Very chronic cases are characterized by increased cornification of the epidermis and atrophy of the rete, corium, and appendages of the skin. The stratum lucidum and stratum granulosum are obliterated in most chronic cases.

Dermatitis exfoliativa is sometimes a fatal affection.

Psoriasis is a chronic affection of the skin characterized by reddish, papular, scaly patches, which are dry, pearly, and lustrous. It affects all ages and both sexes; it may be inherited, and is not infrequent in gouty and rheumatic individuals.

The etiology of the disease is unknown. The pathologic histology is not yet well understood. Sections of the skin show an anomaly of the horny layers, which are thickened, the cells being separated from one another by spaces in which are found various bodies supposed to be nuclei of epithelial cells or of leukocytes, and granular aggregations resembling cocci. It seems to be the presence of the air in these spaces that gives the skin its silvery luster. The cornification of the hyperplastic cells is irregular and often imperfect, so that the lower third retain their nuclei and staining qualities. Keratohyalin and eleidin are nearly absent from the horny and lucid layers, while the granular layer is sometimes thickened, and rarely absent. The cells of the rete usually proliferate, and the interpapillary processes enlarge and extend downward. The corium is moderately inflamed and is somewhat infiltrated with round-cells, the papillæ being enlarged and sometimes deformed.

The hair-follicles and sweat-glands may show distinct changes, though the sebaceous glands are usually normal.

Lupus erythematosus, a chronic inflammatory affection of the skin characterized by hyperemia and thickening, was formerly confounded with lupus vulgaris or tuberculosis of the skin. It is now known to be an entirely independent affection, in which no tubercles are formed, and the lesions of which are simply those of chronic inflammation. The changes chiefly affect the upper part of the corium, in which a proliferation of connective tissue and infiltration of leukocytes occur chiefly about the vessels and glands. Single cells degenerate by fatty and colloid metamorphosis. There is marked chronic hyperemia, and not infrequently obliterative endarteritis may be observed. The glands of the skin are stimulated to overaction in the beginning, but as the disease becomes chronic, they may atrophy.

Tumors of the Skin.—Fibroma is a rare tumor of the skin. It is usually well circumscribed. It may be sessile or pedunculated; in the latter case it may be pendulous. *Keloids* are common in the skin and always succeed traumatic injuries. They are much more frequent in negroes than in Caucasians.

Fibroma molluscum is the most frequent form of cutaneous fibroma. It is sometimes called *neurofibroma molluscum*, because nerve-fibers are said to have been traced into the lesions, which are at times painful. The disease is said to occur chiefly in persons of mental and physical deficiency. The tumors are usually multiple, in some cases thousands occurring simultaneously. They vary in size from a pin-head to a hen's egg, and are usually pedunculated and polypoid.

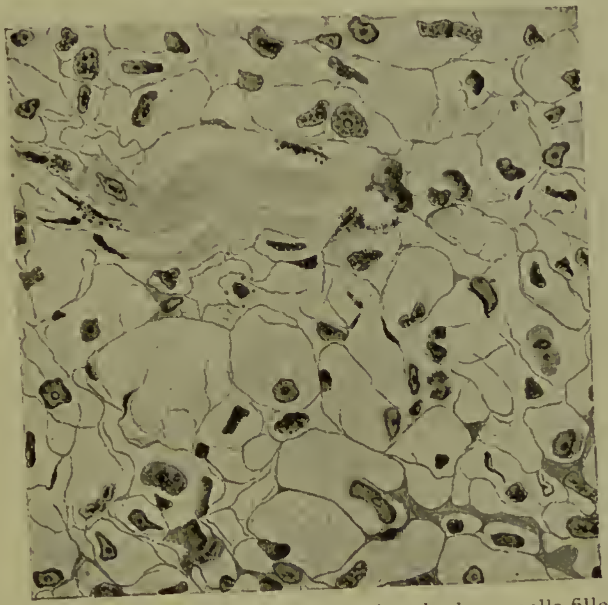

FIG. 286.—Section through a xanthoma nodule, showing the large cells filled with fat-droplets, similar to those composing the sebaceous glands.

Myoma of the skin is very rare and springs from the corium. In general it resembles fibroma. The muscle-cells of the erectores pili and of the vessels are supposed to be the starting-point.

Neuroma is rare, most of the described tumors being *neurofibromata*, or simple fibrous molluscum. Duhring has, however, described a case in which a tumor of the skin consisted of a connective-tissue framework rich in non-medullated nerve-fibers.

Xanthoma, or **xanthelasma,** is a peculiar yellowish-brown discoloration (*xanthoma planum*) or nodular elevation (*xanthoma tuberosum*) usually making its appearance about the eyelids, though occasionally upon other parts of the body. It is essentially a growth of the connective tissue, but is characterized by peculiar cell-nests the nature of which is obscure. These cells, epithelioid in type, are large, seem to possess a cell-wall, and are thickly infiltrated with fat-granules. Unna finds that the fat-granules do not respond to the usual microchemic tests for fat, and it is not improbable that the granules are of some other material. The cells are grouped about the vessels of the corium, sometimes extending as high as the rete. The epiderm may be thinned and its cells vacuolated.

Politzer thinks the fat-cells result from metamorphosis of the muscle-cells of the orbicularis palpebrarum.

Xanthoma not infrequently accompanies systemic disorders, such as jaundice and diabetes (*xanthoma diabeticorum*), though it is not known that these affections have any definite etiologic rôle.

Angioma.—The various forms of nevi already described in Part I. are found in the skin. Of these, the *nævi vasculosi*, or "birth-marks," are most frequent. The soft warts, known as *nævi vasculosi tuberosa*, closely resemble endotheliomata in structure. *Cavernous angiomata* are not common in the skin. Simple telangiectasias are frequent in the form of *rosacea* upon the faces of those who are exposed to the weather.

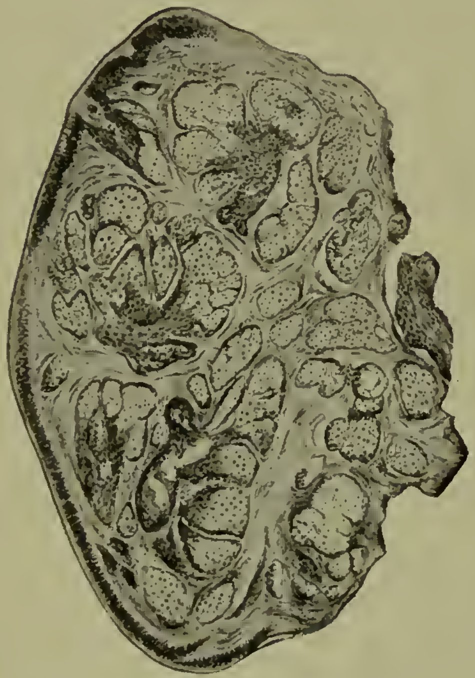

FIG. 287.—Adenoma. The tumor, about the size of a pea, developed from the sebaceous glands of the nose.

Pigmented angioma (*angioma pigmentosum et atrophicum* or *xeroderma pigmentosum*) is a rare form of tumor seen in childhood, which later develops into a malignant growth similar to carcinoma or sarcoma.

Lymphangioma resulting from dilatation of the lymph-vessels is not uncommon, and is usually associated with vascular dilatation. They may form nodular swellings, extensive thickenings, or active elephantiasis. Occasional pigmented forms are observed (*nævi pigmentosi prominens, verrucosi, papillomatosi*).

Lymphangioma occurs in circumscribed form upon the face and head, and not infrequently upon other parts of the body. Elephantiasis usually occurs about the genitals and lower extremities.

Hypertrophic lymphangioma is associated with cellular proliferation and passes imperceptibly into endothelioma of the skin.

Endothelioma of the skin develops in the form of small nodular masses (*endothelioma tuberosum*). The tumor is characterized by tubular masses of endothelial cells developed from the blood or lymph capillaries. Some of the soft warts show this structure.

Sarcoma of the skin is of rare occurrence, and is usually secondary to deep-seated tumors. There are no essential peculiarities.

Melanotic sarcoma of the skin may develop from pigmented nevi, or in rarer cases from the normal skin. The primary tumor may exist for a considerable time and ulcerate before metastases are observed. Melanotic sarcoma of the skin is said to impart metastasis to the lymph-glands, but it is not improbable that many cases in which this has happened have really been epithelial tumors.

To the naked eye, the growths are usually very black. The tumor is very malignant and terminates fatally.

Unna and Gilchrist believe that all pigmented tumors of the skin are epithelial in nature, and that melanotic sarcoma of the skin should no longer be described.

Cancer of the skin usually takes the form of *squamous epithelioma* (*q. v.*). Montgomery divides these tumors into *lobulated* and *tubular* forms. The *lobulated* form is characterized by descending, dividing, and branching processes from the rete, forming nests of every conceivable shape, being modified by pressure. Many epithelial pearls are formed.

The *tubular* form is characterized by processes of cylindric shape which extend at varying angles through the cutis and subcutis. Cell-nests and pearls are not common. This form of carcinoma of the skin has been thought to originate from the sweat-glands, but this is not certain. The *rodent ulcer* is a superficial form of this tumor.

Paget's disease (*q. v.*) is a superficial form of skin cancer seeming to begin in a chronic inflammation of the skin, usually of the areola about the nipple, though sometimes elsewhere. For a long time no other changes are seen in the skin than those depending upon chronic inflammation.

Lenticular carcinoma of the skin usually occurs secondarily to mammary carcinoma in the form of small, multiple, nodular lesions, which eventually unite to form extensive sclerotic areas, such as constitute "*cancer en cuirasse.*"

Pigmented carcinoma of the skin may originate from normal skin or from pigmented nevi and moles. The lesions may be single or multiple, and are intensely black. Early metastasis usually occurs to the lymphatic glands and to the internal organs.

DISEASES OF THE APPENDAGES OF THE SKIN.

The Sweat-Glands.—Hidradenitis suppurativa is an inflammatory disease of the sweat-glands associated with suppuration. It is usually observed where the glands are exceptionally large, as in the axillary and genital regions. The lesions resemble furuncles and end in the destruction of the gland.

Sudamina is an obstructive disorder of the sweat-glands seen in typhoid and other fevers, and characterized by the formation of vesicles in the horny layer. Each is a retention cyst of temporary nature, caused by the accidental plugging of the duct of the sweat-gland and the retention of its contents, or the escape of the contents of the plugged duct between the layers of horny epithelium. Masses of micrococci, supposedly skin cocci, have been found in the duct of the gland.

Miliaria, or **prickly heat,** is an acute affection, common in hot weather when the clothing irritates the skin to undue activity, and free evaporation of the perspiration is prevented. The lesions consist of papules and vesicles of rapid formation, with hyperemic surrounding tissue. The occlusion of the duct is supposed to depend upon the inflammatory swelling. Miliaria differs from sudamina in that it is inflammatory.

Hidrocystoma is similar to miliaria, but more rare. The sweat-glands are permanently obstructed and cystic, and the lesions usually appear on the face in groups. They are the size of sago-grains, and in the corium form cysts, caused by dilatations of deeper portions of the sweat-glands than are affected in either sudamina or miliaria. The cysts contain clear fluid and granular matter.

Diseases of the Sebaceous Glands.—Seborrhea, or oversecretion of the sebaceous glands, occurs in an oily and a dry form.

Seborrhœa oleosa appears to be an excessive production of the sebum, which is purely functional and unattended by anatomic alterations.

Seborrhœa sicca is supposed by Unna to be of parasitic nature and to depend upon the irritation of bacteria. Kaposi believes it to be non-inflammatory and largely functional, depending upon the discharge of the sebum from the glands with considerable admixture of fats and epithelial cells. The disease is most common upon the scalp, where it forms the ordinary *dandruff*, or *pityriasis simplex*. When the condition persists for a long time, it is apt to lead to atrophy of the hair-follicles and permanent alopecia.

Asteatosis is a dry, scaly condition of the skin depending upon absence or constant removal of the sebaceous secretion.

Comedo, or plugging of the ducts of the sebaceous glands, is a frequent affection of adolescence. The outlets of the sebaceous glands are obstructed by plugs composed of inspissated sebum, lanugo hairs, cholesterin, fat, and horny cells, the mass being detected upon the surface of the skin as a dark spot in which Unna claims to have found *ultramarine* pigment. The exact mechanism of the formation of the plug is unknown. The disease is most frequent in patients suffering from digestive disorders and from constitutional vices.

Milium is a somewhat similar affection, in which a more considerable mass of sebum is retained as the result of occlusion of a sebaceous duct. The retained secretion consists of fat and degenerated cells surrounded by an envelop of horny cells. The entire mass is easily enucleated.

Wens, steatomata, sebaceous cysts, or **atheromatous cysts,** are retention cysts of the sebaceous glands which become greatly hypertrophied and surrounded by a connective-tissue capsule. The obstruction may be inflammatory or may consist of inspissated secretion. The contents of the cysts are fatty, with degenerated epithelial cells, cholesterin, and fine hairs. Doubtless many so-called wens are small dermoid cysts.

Wens usually appear about the scalp, though they are not uncommon upon the face and may occur upon the body and limbs. They may attain the size of an egg. They not infrequently inflame and cause considerable pain.

Acne or **acne vulgaris** is an inflammatory disease of the sebaceous glands and surrounding tissues, sometimes limited to one gland, more commonly affecting a gland and its hair-follicle, sometimes affecting several glands and the intermediate tissue. The disease usually occurs during adolescence. Its cause is not known, though it is commonly attributed to digestive disorders and constitutional vices. It may be infectious. The lesions, which take the form of pustules, usually occur upon the face, but may occur upon the trunk and arms. It is one of the most frequent skin-diseases. When the lesions are deeply seated, hard, and do not suppurate, the condition is described as *acne induratum.*

Usually the inflammation terminates in suppuration, the little abscess "points" as a "white head," which, when ruptured, discharges a mixture of pus and sebum, the latter often forming a central cylinder. The lesions usually recover without destruction or with the loss of the follicle, but may be quite destructive, leaving disfiguring pits on healing.

Diseases of the Hairs and Hair-follicles.—The whitening of the hair, so characteristic of advanced age, but sometimes coming on as the result of psychic disturbances and neurasthenia during early life, has been shown by Metschnikoff to depend upon the activity of certain ameboid mesoblastic cells with active phagocytic tendencies, by which the normal pigment of the hair medulla is transferred to the cells about the papillæ. The presence of air or other gases in the hair Metschnikoff found inadequate to account for the change in color, as had been previously taught.

Hypertrichosis is excessive development of hair over all the body. It leads to a Simian appearance, or to the "dog-faced" men. Long, coarse hair has been observed over all parts of the body except the palms of the hands and soles of the feet. It may be congenital.

Alopecia is a condition in which the hair is deficient or absent. It may be congenital, but is usually acquired. Its affects the scalp chiefly in the form well known as *baldness*, but may occur upon any hairy part of the body. The congenital form is usually accompanied by defective development of the nails and sometimes of the teeth. The senile form, chiefly affecting the scalp, is accompanied by atrophy of the hair-follicles. *Premature alopecia* may depend upon seborrhea (*q. v.*); it is sometimes hereditary. Recently it has been taught, and seems to have been demonstrated, that it depends upon infection of the hair-follicles by a particular micro-organism.

Toxic alopecia is observed in some of the infectious diseases, such as syphilis and typhoid fever, in which the hair falls but soon grows in again.

Alopecia areata is usually supposed to be the effect of a trophoneurosis. The hair falls out in irregular areas. As some of the cases occur in epidemics and as there is considerable evidence that the affection is contagious, there is good reason to believe that it is infectious, and, indeed, Sabouraud has constantly found a certain bacillus in the upper third of the diseased hair-follicles, these bacilli being apparently the same as those occurring in seborrhea. With cultures of this bacillus he claims to have produced the disease in calves, rabbits, and guinea-pigs.

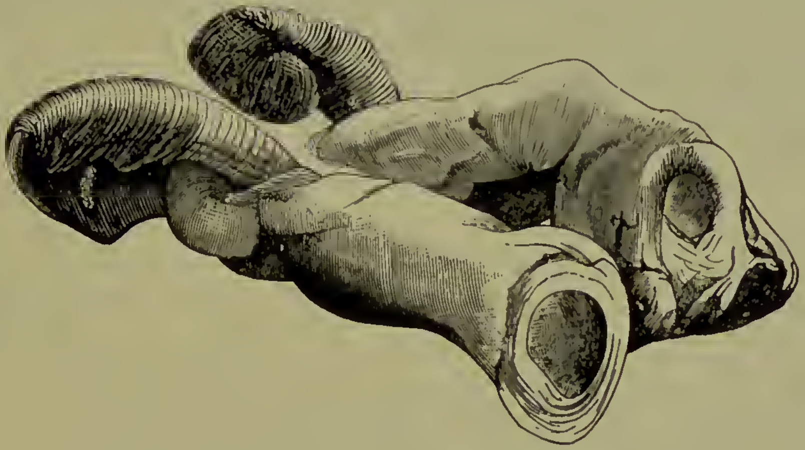

FIG. 288.—Onychogryphosis of toes; natural size (after Ziesing).

Alopecia decalvans is an inflammatory disease succeeded by atrophy of the hair-follicles in groups. It is a slowly progressive disease, lasting for years. When situated upon the back of the neck, it is sometimes known as *dermatitis papillaris capilliti*.

Atrophy of the hair is often the precursor of *alopecia prematura*. It seems to depend upon some systemic disturbance of nutrition. It also occurs in numerous local diseases, such as eczema and seborrhea. The hairs become lusterless and dry, and split and fracture. Their caliber also becomes smaller. Dry brittleness of the hair is known as *fragilitas crinium*.

Trichorrhexis nodosa is a rare atrophic disease of the hairs, usually of the beard, in which swellings or nodes occur here and there upon them, fracture easily occurring at these points, the ends being frayed out. The disease is doubtless parasitic.

Monilothrix is a congenital and often hereditary affection in which the hairs show constrictions, at which points they are prone to fracture.

Diseases of the Nails.—**Hypertrophy of the nails** or **onychauxis** is not infrequent. The nails become thick, rough, uneven, brittle, and lusterless. They are often elevated from the nail-bed. The color changes and usually becomes a dirty yellow-brown. When the nail is bent over the finger-tip like a claw, the condition is described as *onychogryphosis.*

Horns upon the nails are not uncommon (see Horns).

Atrophy of the nails is characterized by thinning, softening, furrowing, and ridging. The tissue becomes brittle, has a tendency to split, and is sometimes discolored. Transverse furrows across the nails are not uncommon in atrophy. Such furrows are not infrequently developed during systemic affections, such as typhoid fever, etc., and depend upon temporary malnutrition. *Leukopathia unguium,* or white spots on the nails, usually depends upon slight traumatic injuries, though it may mark systemic depravity.

Hyperkeratosis is seen in syphilis, leprosy, tuberculosis, acromegaly, myxedema, neuritis, eczema, etc. It is characterized by an accumulation of imperfectly cornified cells at the bed of the nail. The nail is thus partly elevated, softened, and moistened. Bacteria not infrequently grow in the porous tissue and cause it partly to putrefy and become offensive. The nails may be temporarily or permanently shed in consequence.

Onychitis, or inflammation of the matrices of the nails, may result from traumatic injury and from infection. It usually terminates in the exfoliation of the nails, which soon, however, reform, unless the matrix be destroyed by suppuration. Onychitis or *onychomycosis* sometimes results from the growth of the favus fungus (Achorion schönleinii) at the root of the nail.

Loss of the nails results from hyperkeratosis, onychitis, paronychitis, syphilis, alopecia areata, diabetes, etc. It not infrequently follows traumatic injury with subungual extravasation of blood.

CHAPTER VI.

DISEASES OF THE SPLEEN, LYMPHATIC NODES, THYMUS GLAND, AND BONE-MARROW.

THE SPLEEN.

Congenital Malformations.—*Total absence* of the spleen is very rare, but has been seen occasionally in acephalic monsters and other markedly defective individuals. It has also been seen in a few otherwise well-formed persons, probably the oldest cadaver in which it was absent being a three-year-old child examined and reported upon by Roberts.

The spleen sometimes takes the form of a collection of rounded, pea- and cherry-sized bodies, fastened to a peritoneal fold corresponding to the gastrosplenic omentum. Less marked anomalies, such as lobulation, notching, etc., are very common.

Not infrequently *accessory* or *supernumerary spleens* are observed. These are usually the size of a pea, or may be as large as a cherry. They may be single or multiple, and are situated in the neighborhood of the spleen in the folds of the peritoneum. They are readily recognizable by their color and consistence. Marsh observed two quite well-formed spleens in the same person.

Not infrequently the spleen is abnormally movable, and in consequence assumes unusual positions. Such cases are spoken of as *floating spleen*, and most usually depend upon existing or previous enlargement of the organ, which has stretched its attachments, or upon congenitally long attachments.

Anemia.—The spleen may appear anemic in general anemia, in cases of considerable loss of blood from hemorrhage, and in inanition. The anemic organ is smaller, paler, and denser than normal, and has a wrinkled capsule. When incised, it is found to be of a reddish-brown or slate color, and firm and fibrous.

Hyperemia.—**Active hyperemia** of the spleen is of very frequent occurrence. It is seen in those who die after partaking of a hearty meal, probably occurring at the same time as the digestive leukocytosis. It is also almost invariable in the infectious diseases. The organ manifests its hyperemic condition by increase in size, stretching of the capsule, the dark-red color of its cut surface, the soft or even mushy consistence, the softened, protruding parenchyma of the trabeculæ, and the less distinct Malpighian corpuscles.

Passive hyperemia of the spleen is the result of disease associated with circulatory obstructions. It is observed in cirrhosis of the liver, chronic cardiac diseases, emphysema, etc. The spleen is enlarged, and its capsule tense and elastic; the color is dark reddish-black and the pulp soft. As the condition progresses the capsule of the organ thickens, and the fibroconnective tissue increases so that the trabeculæ become thickened. The ultimate outcome of the process is diminution in size, firmness, and pallor. Actual atrophy of the splenic pulp seems to take place, and pigmentation of its tissue is quite common.

Hemorrhage into the spleen usually results from traumatism, and is chiefly subcapsular. The most frequent form of hemorrhage is *hemorrhagic infarction* and follows embolism. Small punctate hemorrhages occur in the spleen in the infectious diseases. If the spleen be congested, they cannot be recognized.

Embolism of the spleen is frequent, and is characterized by both hemorrhagic and anemic infarction. In hemorrhagic infarction conic areas of tissue with the base directed toward the capsule and the apex at the hilus either become entirely suffused with blood or are somewhat pale in the center and saturated with blood at the periphery.

The anemic infarct differs in that the tissue is pale, anemic, and necrotic. The usual termination is necrosis, gradual absorption, reactive inflammation, cicatrization, and contraction, so that ultimately nothing remains except a deep dimple with a fibrous cicatrix at its bottom.

Thrombosis of the splenic vein causes the organ to become much swollen. It rarely occurs except in connection with thrombosis of the portal vein.

Inflammation of the spleen is a condition which, in its milder grades, is very difficult of recognition because of the peculiar structure of the organ, making it almost impossible to determine the existence of those features regarded as essential to inflammation—viz., inflammatory hyperemia and round-cell infiltration.

Infection.—In nearly all the infectious diseases the spleen undergoes a marked enlargement, forming what is clinically known as *splenic tumor*, or when associated with malaria, *ague-cake*.

In such cases the spleen is large, soft, elastic, dark colored, and mushy. Its substance, exposed by a clean incision, is sometimes dark grayish-red, reddish-black, or blackish. It is homogeneous, and the trabeculæ and Malpighian corpuscles are invisible. The structure is soft and easily lacerated or penetrated with the finger, while it readily gives up its substance when scraped with a knife.

Microscopically, the appearance of such splenic tissue is quite uniform in the various conditions in which it occurs. The veins and other distinct blood channels are engorged, the spaces of the vascular meshwork and splenic pulp distended with a cellular collection composed partly of erythrocytes, but chiefly of polymorphonuclear and lymphocytic leukocytes. There are also a number of large. rounded, mononuclear cells, often containing numerous erythrocytes which they have incorporated in their protoplasm. These cells, as do also the lymphocytes, undoubtedly multiply during the splenic enlargement, as many karyokinetic figures can be observed. Exactly what the nature of this change in the splenic pulp is has not yet been determined. It is supposed that active phagocytosis is in progress in the organ, this view being favored by the results of numerous researches which indicate that bacteria and other minute particles circulating in the blood are gathered in the spleen and there destroyed.

That the importance of the changes is not so great as to make them indispensable may be determined by observing that the removal of the spleen is not attended with important changes in either man or animals, and does not increase their susceptibility to disease or prevent recovery. As the splenic enlargement runs a course parallel with that of the infectious process, increasing until the acme of the disease is reached and then diminishing as the disease declines, it seems almost certain that the changes depend upon the specific bacteria or micro-organisms of the diseases. This is further substantiated by the fact that certain of the toxic diseases produce tissue necrosis in the spleen. Among these may be mentioned pyemic infection, diphtheria, recurrent fever, typhoid fever, etc.

The enlarged spleen may reach three or four times its usual bulk. The capsule may burst from the swelling of its contents. Suppurations, hemorrhages, and fatal peritonitis may occur.

When the number of leukocytes contained in the splenic pulp exceeds the number of erythrocytes, so that the pulp has a grayish color and is soft and swollen, the organ is said to be inflamed and the condition is described as *splenitis*. If the capsule of the organ be inflamed, the condition is described as *perisplenitis*.

The swollen spleen of an infectious disease remains enlarged and softened until convalescence, when a gradual reduction, depending upon the destruction and absorption of the cells or their return to the blood, occurs, and finally the organ is restored *ad integrum*. It is usual to find atrophy following the excessive enlargement in such cases, and it is doubted by some whether the spleen, when once considerably enlarged, ever does return to its normal size and appearance. Indeed, there is so much alteration in the capsule and such marked changes in the trabeculæ that more or less induration seems to follow of necessity.

In malaria, in which the enlargement of the organ is frequently repeated and long continued, a true hypertrophy of the spleen, with hyperplasia of the pulp tissue and more or less marked pigmentation, nearly always occurs.

Not infrequently, in consequence of perisplenitis depending upon lesions of the capsule from overstretching, fibrous adhesions form between the spleen and neighboring organs.

Purulent Inflammation of the Spleen.—Acute splenitis of a suppurative character results from hematogenous infection with pyogenic bacteria, from splenic infection in septicemia and typhoid fever, and from the extension of suppuration from neighboring parts. It very commonly takes place from infectious emboli with infarctions which rapidly suppurate. The abscesses which form may be single or multiple and vary in size. The appearances need no special description. The suppuration terminates either in absorption of the exudate or in rupture and evacuation into the peritoneal cavity or into the stomach, intestines, pleura, lung, etc.

Chronic Splenitis.—Chronic interstitial inflammatory alterations of the spleen are observed in chronic cardiac disease, cirrhosis of the liver, etc., in which there is a persistent passive congestion of the organ; in infections with prolonged course or repeated attacks, as malaria; and in certain systemic affections accompanied by general tissue alterations, such as syphilis and rickets.

The essential feature of the process is fibroconnective-tissue induration, which increases the size of the trabeculæ, thickens the capsule, and reduces the size of the organ. When incised, the pulp appears paler than usual and the trabeculæ are unusually prominent. The organ is firmer than normal.

Tuberculosis of the Spleen.—Primary tuberculosis of the spleen is rare. Miliary tuberculosis, on the contrary, is most frequent and occurs in almost every case of advanced pulmonary tuberculosis. Miliary tubercles appear as minute grayish points not much larger than the Malpighian corpuscles, and easily mistaken for them. Older tubercles are invariably caseous and softened in the center. They vary in size from a pin-head to a cherry, and are yellowish in color. Tubercles may occur both in the substance of the organ and in the capsule.

Leprosy of the spleen is very rare and is characterized by small cellular nodes. Complicating tuberculosis is common in leprosy, and care must be exercised that the lesions are not confused.

Syphilis of the spleen is usually characterized by the formation of gummata. It is a rare affection, but may occur in both acquired and hereditary syphilis. The gumma is usually multiple, and may be present in considerable numbers. They appear as grayish, transparent nodes, which later become opaque, yellowish in the center, with a grayish surrounding zone of connective tissue.

Diffuse hyperplasia of the connective tissue is an almost constant alteration in congenital syphilis. It also occurs in the acquired form of the disease.

Atrophy of the spleen is very common in senility. The organ is small, wrinkled, pale, flabby, and pigmented.

Atrophy may also result from exaggerated perisplenitis with callous formations in the capsule.

Degeneration.—Amyloid disease has a marked predilection for the spleen, affecting it more frequently than any other organ. The amyloid disease first affects the walls of the blood vessels and contiguous cells, and can first be observed in the Malpighian corpuscles, which become enlarged, pale, grayish, and translucent, forming bodies somewhat comparable to grains of sago. A spleen with such a degree of amyloid disease is described as *sago spleen*. When more advanced, the process becomes diffuse and affects all the structures of the spleen, causing it to enlarge to several times its normal size, and somewhat to resemble bacon in appearance. The borders of the organ are rounded and much thicker than normal. On section, the tissue is anemic, dense, inelastic, friable, and of a pale-brown color.

Pigmentation of the spleen occurs in chronic congestion, especially that from cirrhosis of the liver, from diseases associated with hemolysis, from repeated attacks of acute splenic enlargement, and from malaria. In old people the spleen is usually somewhat pigmented. The color of the organ varies from red brown to dark brown or even black. The entire substance may be pigmented, or it may have irregular mottlings from peculiarities of the pigment distribution. The pigment-granules are first observed in the walls of the blood vessels, then in the vessel-walls and surrounding cells, and finally in the cells of the parenchyma.

The pigment found in congestion and in hemolytic anemia is hemosiderin ; that found in malaria is melanin.

Anthracosis sometimes occurs in the spleen, as in other deep seated organs, from the entrance of coal-pigment into eroded veins.

Calcification of the spleen is occasionally observed in old infarcts, in thickenings of the capsule, in old tuberculous and gummatous lesions, and rarely in echinococcus cysts.

Leukemia.—The alterations in the spleen in leukemia and pseudoleukemia, or Hodgkin's disease, are identical. The essential characteristic is hyperplasia of the parenchyma, by which the organ attains an enormous size, weighing from 5 to 10 kilograms.

To the naked eye the spleen is greatly enlarged and its capsule thickened. Its substance shows more or less circumscribed fibrous thickenings, some of which are almost cartilaginous in density. Scars are often observed, some from partial lacerations of the capsule, some because of the presence of infarctions and necroses. The organ is soft in the early stages of the disease, but becomes firm and dense in chronic cases. Local areas of softening, depending upon interstitial hemorrhage or necrosis, may be present.

The appearance of the incised organ varies according to the structures affected, the extent of the disease, and the complications that may exist.

In mild cases of leukemia or in the early stages of the disease the changes may be observed chiefly in the Malpighian corpuscles, which, by hyperplasia of the lymphoid tissue, become very greatly enlarged, pale in color, and stand out conspicuously, forming the *sago spleen*. As the disease advances the interfollicular lymphoid tissue undergoes hyperplasia, and general enlargement occurs, together with induration, and a condition frequently characterized as the *second stage* of the process develops. The cut surface of the organ may be reddish or brownish in color, but presents interesting variegations, areas of yellowish necrosis, whitish or grayish nodular masses of lymphoid tissue, interstitial hemorrhages, and infarctions giving the whole a marbled appearance—*marbled spleen.*

When the enlargement becomes very great, the capsule of the spleen may rupture, causing fatal hemorrhage or peritonitis.

Tuberculosis and other complications sometimes occur simultaneously with leukemia, and modify the pathologic appearances. When studied microscopically, it is found that the lymphoid tissue has undergone a marked hyperplasia, and that the cells are, to a more or less marked extent, in process of karyokinesis. The newly formed cells conform, as a rule, to the preexisting cells of the organ, but sometimes cells of unusual size are found mixed with the mononuclear and polynuclear cells. Giant-cells are occasionally seen. The interfollicular cells are frequently in a condition of granular necrosis. The cellular hyperplasia occurs not only in the pulp, but also invades the trabeculæ and walls of the smaller blood vessels. The pulp itself is usually congested. In very chronic cases the original lymphatic hyperplasia gives place to fibroid indurations, and in the follicles the original structure may be entirely lost.

Banti's Disease.—The enlargement of the spleen that accompanies *cirrhosis of the liver*, especially the hypertrophic form, closely resembles the spleen of leukemia in appearance, but does not show the same enlargement of the Malpighian corpuscles. In this disease the spleen may weigh as much as 1200 grams. The enlargement may occur when venous obstruction is absent. The pulp is hyperplastic and hyperemic, and in chronic cases with marked enlargement may contain cellular connective tissue. Splenic cells in a state of fatty degeneration are observed in the pulp.

Tumors of the Spleen.—**Primary tumors** of the spleen are rare. Rokitansky, Lancereaux, and others have observed small, rounded, encapsulated tumors, the structure of which was identical with the spleen itself and to which they have applied the name *adenoma of the spleen.*

Of the primary connective-tissue tumors, *fibroma*, *sarcoma*, *angioma*, and *lymphangioma* have been observed.

Secondary tumors of the spleen are common, and in generalized sarcoma and carcinoma one expects to find secondary growths in the spleen. The form of these growths is usually that of multiple rounded nodes, superficially or centrally situated.

Cysts of the spleen are infrequent. Very small cysts may occasionally arise from follicular degeneration. Larger cysts may be formed in consequence of lymphatic obstruction and ectasis. Large serous cysts may also result from inclusions of peritoneal endothelium during embryonal development. Very large cysts—as large as a child's head—may sometimes be formed in cavernous lymphangiomata and other tumors.

Dermoid cysts are rare in the spleen. Andral has, however, reported the occurrence of a cyst, presumably a dermoid, containing hair.

Parasites of the spleen are rare. The *Pentastomum denticulatum* is occasionally seen inclosed in a small cyst close beneath the capsule. It is usually calcified.

The *cysticercus* is rarely observed in the spleen.

The *Tænia echinococcus* not infrequently infects the spleen and forms typical cysts with numerous daughter cysts. It may cause great increase in the size of the organ.

Actinomycosis has been observed in the spleen.

Rupture of the spleen may result from traumatism, or may occur spasmodically in diseased conditions with increase in size and inelasticity of the capsule. It may recover by cicatrization and the formation of a linear or stellate capsular scar, but usually leads to hemorrhage into the abdominal cavity and death.

Calculi of the spleen occur in consequence of the calcification of thrombi, etc. They are more correctly described as *phleboliths* than as splenic calculi.

DISEASES OF THE LYMPHATIC NODES.

Anemia.—In general anemia the nodes are shrunken and drier than normal.

Hyperemia is indicated by a pinkish or reddish color, increased size, and unusual juiciness of the nodes. The hyperemia seems to occur more frequently in the capsular and cortical part of the organs than toward the center. Hyperemia is usually the precursor of inflammation.

Atrophy of the lymph-nodes takes place in old age. It starts in the lymphocytes of the medullary substance, which gradually disappear, beginning in the neighborhood of the hilus and leaving the connective-tissue framework, which is slowly transformed into adipose tissue. This is best seen in the mesenteric nodes. Not only the lymphatic nodes, but also the lymphatic follicles of the mucous membranes, atrophy in advanced life.

Hypertrophy of the lymphatic nodes takes place in the peculiar affection usually classified among the tumors, and known as *lymphadenoma*.

Amyloid disease of the lymph-nodes occurs with amyloid disease of other organs of the body, from chronic tuberculosis, etc. The condition first shows itself in the walls of the small blood vessels. When present in marked degree, the nodes may be dull gray-white, firm, and somewhat enlarged. The amyloid substance may be found in the nodes or in the cords and sinuses.

The process seems first to affect the framework, the component fibers and cells of which become thickened, bulbous, and irregular and may fuse to form masses. Some of the lymphocytes may be included in the amyloid masses and finally disappear.

Hyaline degeneration is occasionally observed affecting the blood vessels and sometimes the cells of the lymphatic nodes.

Calcification of the lymphatic nodes is occasionally seen in old tuberculous and necrotic lesions. The distribution of the calcareous material corresponds to the original distribution of the tubercles, etc.

Pigmentation of the lymphatic nodes is frequent from the collection of internal and external substances. The most frequent hematogenous pigmentation is by hemosiderin, and takes place in the lymphatic nodes in the neighborhood of hemorrhagic extravasations from which the granules of altered blood-pigment are conveyed chiefly by leukocytes. The pigment-granules seen in the gland are principally in the lymphocytes of the sinuses, but ultimately reach those of the lymph-cords and nodes. When but little pigment is present, it can be observed only by careful microscopic examination, but when much is present, it may give the glands a rusty or even a dark-brown color.

Extraneous pigments are observed in the lymphatic nodes in cases of tattooing of the skin and in pneumonokoniosis. The particles of these substances are microscopically recognizable by their color. Extraneous and solid substances in the nodes ultimately cause much induration by connective-tissue formation. Sometimes when masses of coal-dust enter and accumulate within the nodes the tissue softens instead of indurating. *Periadenitis* is also caused by the presence of foreign particles within the nodes.

Dark color of the lymph-nodes of the abdomen may depend upon the presence of blood sinuses, these nodes being described by Gibbes and Warthin as *hemolymph glands*. Their characteristic feature is the presence of the blood sinus, which other lymph-nodes lack. The function of these organs is unknown; it is supposed they have something to do with hemogenesis.

Inflammation, or lymphadenitis, is of frequent occurrence, and is usually of lymphogenic origin, being secondary to neighboring infections, as in chancroidal bubos, but may occasionally be caused by the hematogenous distribution of bacteria. It is sometimes caused by toxic irritation.

There is usually an inflammatory hyperemia and edema, accompanied by swelling and either softening or condensation of the node. The passing currents of lymph wash out the lymphocytes from the sinuses of the node, and more or less desquamation of the endothelial cells occurs. An inflammatory exudate accumulates, varying according to the different degrees or variety of inflammatory reaction. In cases of pyogenic infection of the lymph-nodes from infected wounds, and in such infectious diseases as scarlatina, erysipelas, and plague, in addition to the liquid transudation, there are collections of polynuclear leukocytes which may amount to actual suppuration of the tissue and the formation of larger or smaller abscesses about the micro-organismal emboli. The rupture of these abscesses, or their extension to the surrounding tissue, produces suppurative peri-adenitis. Secondary lymphadenitis also occurs in chancroid, diphtheria, gonorrhea, etc.

In toxic affections, particularly diphtheria, small necrotic foci are observed in the tonsils, in the lymphatic glands of the neck and throat, and also in Peyer's patches and many of the mesenteric nodes. In typhoid fever the necrotic changes are extensive and involve nearly all the tissue of the Peyer's patches and many of the mesenteric nodes.

When the activity of the inflammation is violent, the exudate may be fibrinous in character, or when still more destructive, may be hemorrhagic.

The inflamed nodes are always swollen. Their color varies from pinkish or grayish-red to dark-red when hemorrhagic.

The term *bubo* was formerly applied to swollen nodes of the inguinal region, but the term is no longer restricted to any particular group of nodes.

The recovery of the inflammation is usually by simple absorption of the exudate. The fluid transudate is absorbed, the leukocytes in part return to the circulation, while others, caught in the fibrin network, soften and melt away. Small fragments are taken up by the lymphatic cells. When collections of pus remain without absorption, or when necrotic masses occur in the nodes, a connective-tissue hyperplasia takes place in their immediate surroundings, and large mononuclear cells, probably the offspring of the connective-tissue cells, form and ultimately lead to the formation of encapsulating connective tissue. Isolated abscesses of this kind sometimes calcify. Necrotic masses similarly surrounded may be absorbed and leave nothing but cicatrices in the tissue—*lymphadenitis proliferans* or *indurativa*.

Chronic lymphadenitis may be caused by retained products of inflammation, by tuberculosis, syphilis, lepra, and other chronic, specific, infectious diseases. It also results from progressive pneumonokoniosis, and in the intestine, from chronic irritation from digestive by-products. From this irritative hypertrophy of the nodes considerable induration and fibroconnective-tissue formation may occur.

Tuberculosis of the lymphatic nodes sometimes occurs as a primary hematogenous infection. As a rule, however, the tubercle bacilli are carried to the node by the afferent lymph-vessels, so that the disease is secondary to some neighboring focus, as the intestinal ulcer, which infects the mesenteric node, the lung, and the bronchial nodes. Primary lymphogenic tuberculosis also occurs from lymphogenic infection without primary disease at the point of bacillary entrance. Such cases are best illustrated in the cervical node infection, which probably occurs through the uninfected tonsil, in the mesenteric node tuberculosis, and in the primary tuberculosis of the bronchial nodes.

To the older clinicians the tuberculous nodes formed part of the condition described as *scrofulosis*, but abundant and conclusive evidence, both histologic and experimental, has now shown the disease to be identical with tuberculosis. The scrofulous nodes are particularly common in childhood, antedating puberty. Those most frequently affected are the cervical, mesenteric, bronchial, and tracheal groups. The nodes are enlarged, sometimes movable beneath the skin, though they may be adherent to the skin and to neighboring glands and structures. They may be soft and caseous, and may rupture and discharge externally through the skin or into neighboring cavities. When dissected out and examined, they are grayish or reddish in color. There may be single tuberculous masses or numerous miliary or caseous tubercles scattered throughout the node, appearing as yellowish or grayish spots. The caseation begins in the central part of the tubercles and extends, as the tubercles increase in size, until the entire substance of the gland is transformed into a softened, semifluid, creamy mass. As the tuberculous process advances, distinct signs of regeneration take place in the glandular tissue in the form of connective-tissue proliferations. These undoubtedly begin in the proliferation of the preëxisting connective-tissue cells of the trabeculæ, forming large, mononuclear, rounded cells, which seem to be the early form of the fibroblasts from which connective tissue is formed, the surrounding tissue being indurated so as to shut in the tubercle and render its extension difficult.

The process either advances rapidly and is accompanied by much softening and degeneration, with infiltration of neighboring tissues and frequent external rupture, sinus formation, and slow stellar cicatrization, or is slow and accompanied by marked connective-tissue induration, encapsulation, and sometimes calcification of the tuberculous tissue.

Lymphatic node tuberculosis is one of the most benign forms of the disease, and the patient frequently recovers perfectly. By continuous extension along the lymphatic chain, by infecting important organs, by continuity of tissue, by intravenous rupture, by systemic distribution of bacilli, and by the production of general miliary tuberculosis the disease may prove fatal.

Calcification of tuberculous nodes is common in the mesentery. Tuberculosis of the mesenteric nodes was described by the older clinicians as *tabes mesenterica.*

Syphilitic lymphadenitis accompanies the secondary stage of syphilis. If the primary sore is situated upon the genital organs, the inguinal nodes are first enlarged (*syphilitic bubo*). The nodes enlarge rather slowly, do not coalesce or become adherent to the skin, but remain freely movable. They usually attain the size of a pigeon's egg. In case the chancre is a soft suppurating sore, the nodes may suppurate, but in all probability in these cases there are associated infections which, rather than the syphilitic infection, are responsible for the suppuration. From these first affected nodes the disease gradually spreads until those of the entire body are enlarged.

Microscopically, the affection is characterized by leukocytic infiltration, thickening of the trabeculæ, and proliferation of the endothelial cells of the lymph-sinuses. The proliferated endothelial cells sometimes take the form of a large-cell hyperplasia which is somewhat characteristic. One of the important microscopic features is that the vessels of the lymphatic nodes show a marked round-cell infiltration in their walls.

In *constitutional syphilis* a general lymphatic involvement occurs, the changes observed in the nodes being similar to those already described.

In *tertiary syphilis* gummata of small size are frequently observed in the lymph-nodes in the immediate neighborhood of organs containing large gummata. Rarely the gummatous nodes coalesce, undergo the gummy degeneration, and form considerable-sized masses.

The degenerated tissue characteristic of gumma is grayish, rarely whitish and gelatinous, and has a peculiar coarse, band-like form which differentiates the disease at once from tubercle.

Microscopically, the gummata are observed chiefly in the lymph sinuses. The lesions have the usual characteristic appearance and contain leukocytes, lymphocytes, proliferated endothelium, etc., all in the condition of fatty and hyaline degeneration.

Lepra, glanders, actinomycosis, etc., with specific infection of the lymphatic nodes, are recognized by their characteristic lesions.

Chancroid is usually accompanied by *bubo*, or enlargement of the inguinal lymphatic nodes. The lesions are suppurative. In them Ducrey's bacillus may be found.

Tumors of the Lymphatic Nodes.—Leukemia.—The lymphatic form of leukemia is characterized by progressive enlargement of the lymphatic tissues of the body. The affection may begin in a single node or simultaneously in a group, and gradually spread from node to node until most of the nodes of the body are affected. There may also be *lymphoid deposits*—as if metastatic—in organs in which no lymphoid tissue is normally present. The disease is associated with characteristic changes in the blood which make its recognition much easier than would otherwise be possible.

The enlarged nodes are usually movable beneath the skin. They may not be much above the normal size, or may be as large as hen's eggs, and form prominent tumors. Macroscopically, they do not differ in appearance from normal lymph-nodes. Microscopically, the lesion consists in a simple hyperplasia of the gland without essential peculiarities.

Hodgkin's disease, pseudoleukemia, adenia, lymphosarcoma, or **malignant lymphoma,** is a peculiar affection in many particulars resembling an infectious disease, in others resembling a neoplasm. The true nature of the affection has not been determined.

The disease occurs in two chief forms, one of which affects single nodes or groups of nodes, the other, all the nodes of the body. It may be a chronic affection lasting for years, or an acute affection leading to a fatal termination in a few weeks. The enlarged nodes are sometimes soft, sometimes hard. These peculiarities cause them to be described as acute, chronic, hard, soft, general, local, etc. Not infrequently they are called *lymphoma*, *soft lymphomata*, and are characterized by rapid growth and wide distribution. The individual nodes may become as large as goose-eggs, and be so soft as to fluctuate. Neighboring nodes coalesce, though the interglandular separations usually remain visible. When incised, the nodes are very soft and permit the exudation of a milky fluid.

The *hard lymphoma* is not usually so large and is firmer, the cut suface being grayish-white or yellowish. Sometimes the tumors have a fibrous appearance. Upon microscopic examination the tissues vary considerably in appearance. As a rule, they closely resemble the enlargements of leukemia—*i. e.*, they are simple hyperplasias in which the structure of the lymphatic node is altered only by an excessive development of lymphadenoid tissue. The cells are chiefly large lymphocytes, but eosinophile cells and very large cells sprinkled through the tissue are common.

In the more malignant forms—soft lymphoma—the cells are often larger, and it is not at all unusual to find giant-cells among the cells of the tissue.

The soft lymphoma also shows a disposition to break through its capsule and extend into the surrounding tissue, thus being more like sarcoma than like leukemia in type.

Tuberculosis of the lymphatic nodes may be mistaken for lymphadenoma, sometimes, however, occurring with it.

Sarcoma of the lymphatic nodes develops from a node or a small group of nodes, and causes the affected organs to unite and form nodular masses. The tumor soon breaks through the capsules of the nodes and infiltration begins in the surrounding tissue, with metastasis to the internal organs. One of the chief characteristics differentiating sarcoma from the lymphoma is its tendency to give metastasis to internal organs without invading other lymphatic glands. It may not be possible to differentiate the primary tumors microscopically.

The sarcomata may be of various varieties, small round-cell, spindle-cell, fibrosarcoma, angiosarcoma, and alveolar sarcoma all having been observed. It seems probable that the different forms of sarcoma grow from different elements of the tissue of the lymph-node.

Melanotic sarcoma is rare.

Secondary sarcoma of the lymphatic nodes occurs by lymphatic extension or by the conveyance of sarcoma cells through the lymphatic vessels. The secondary tumor is like the parent.

Myxoma is occasionally observed in the lymphatic nodes.

Chondroma sometimes occurs secondarily in the lymph-nodes in the neighborhood of primary chondrous tumors.

Secondary carcinoma is one of the most frequent affections of the lymphatic glands, and occurs in the nodes nearest the seat of disease in nearly every case of carcinoma. Its origin no doubt depends upon the transfer of the carcinoma cells from the primary seat of disease to the glands by currents of lymph.

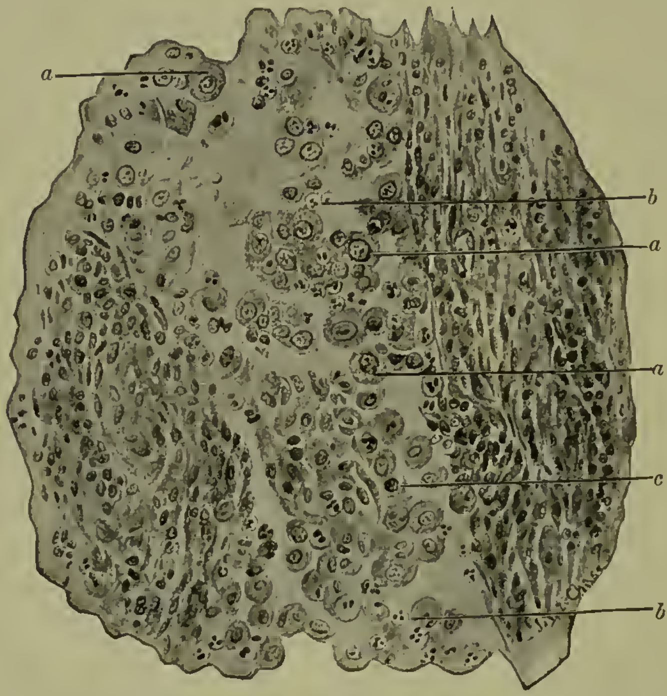

FIG. 289.—Carcinoma of lymphatic node, illustrating metastasis. On the right and left glandular tissue with interstitial fibrous change. Through the center of the illustration is a widely dilated lymph-vessel filled with cells: *a*, *a*, *a*, Carcinoma cells freely circulating in the lymph; *b*, *b*, leukocytes; *c*, lymphocyte.

DISEASES OF THE THYMUS GLAND.

Congenital Malformations.—The thymus gland is rarely absent in otherwise well-formed individuals. Occasionally there are small accessory thymus glands, usually situated high up in the neighborhood of the thyroid. One of the most frequent abnormalities of the organ is its failure to atrophy during the first few years of life, and its persistence until puberty or even until middle life. Rarely the thymus gland is found to be greatly hypertrophied, so as to cover the great vessels and pericardium. This condition is occasionally found in cases of sudden death.

Hyperemia.—In asphyxia the thymus is sometimes found intensely congested and filled with punctiform hemorrhages.

Inflammation of the thymus probably occurs only in hematogenous, pyogenic infection, and is characterized by the formation of small abscesses. Sometimes it is said that the pus accumulates in the original epithelial spaces of the gland. Inflammation may also occur at times from extension from neighboring organs and tissues.

Tuberculosis of the thymus is rare. It may assume the form of miliary tubercles or caseous masses.

Syphilis of the thymus is characterized by gumma formation. The lesion is most frequent in the new-born with hereditary congenital syphilis.

Tumors of the Thymus.—From the lymphatic tissue of the thymus *lymphoma* and *lymphosarcoma* occasionally develop.

Epithelioma sometimes develops from the retained and altered cells of the corpuscles of Hassell.

DISEASES OF THE BONE-MARROW.

Although it can scarcely with propriety be discussed independently of the osseous tissue which surrounds and pervades it, the close relation which the bone-marrow bears to the other lymphoid tissues requires brief consideration.

The bone-marrow is a lymphoid tissue. In early life it is of a bright-red color and soft consistence, and consists essentially of cells with a delicate, intervening reticulum of connective tissue and numerous capillary and venous vessels. The cells are, for the most part, round-cells with bright clear nuclei of a vesicular form, or with indistinct homogeneous nuclei. The bone-marrow also always contains a large number of round-cells with eosinophile granulations in their protoplasm, flattened cells somewhat of the endothelial type, large round adipose cells full of fat, nucleated and non-nucleated red blood-corpuscles, cells containing red blood-corpuscles and pigment, and quite a number of giant-cells.

As the individual becomes older, the marrow in the shafts of the long bones undergoes a marked fatty infiltration and appears bright yellow, while that of the epiphyses and the spongy tissue of the short bones maintains very nearly the original appearance and contains very little fat.

The physiologic function of the red marrow is now generally accepted to be hematogenesis.

Hyperemia.—Whether or not hyperemia of the bone-marrow occurs is not known. If so, it is unimportant.

Anemia.—The essential anemias are accompanied by marked alterations of the bone-marrow. The most important change is seen in *pernicious anemia*, where the fatty tissue of the marrow is absorbed and a return to the primitive condition is observed. Instead of the original bright red, the color is somewhat darker and appears like *raspberry jelly*. The change begins at the epiphyses and extends toward the center of the shaft of the long bones.

In **leukemia** the condition is somewhat different, and the marrow is more of a grayish color, and is frequently mottled or speckled, the pale-gray areas consisting chiefly of leukocytes actively proliferating; the darker red areas of more normal marrow, congested and extravasated. Sometimes the paler areas resemble purulent collections, so that the term "*pyoid marrow*" is used in describing them.

It is generally believed that the bone-marrow is the origin of the myelocyte of leukemia, and large numbers of them are present in it. More rarely the marrow in leukemia is all red, and resembles that of other anemic conditions. Charcot-Neumann crystals are frequently found in the marrow.

The marrow changes are naturally most frequent and most typical in the myelogenic form of leukemia. In the lymphatic form they may be purely the result of the secondary anemia present.

Atrophy of the bone-marrow is seen in senile and marasmatic conditions. It is characterized by absorption of the fat, diminution in the number of cells, and not infrequently by retrogressive changes in the tissue elements, by which they become mucilaginous—*myxomatous* (?) *degeneration.*

Hypertrophy.—The change in the bone-marrow in anemia may be regarded as a hypertrophy. As, however, it is more a return to the primitive condition, it seems best to speak of it under Anemia.

Degenerations.—*Fatty infiltration* is a normal process which begins shortly after birth and continues up to about the sixteenth or eighteenth year. Sometimes it occurs in excess of the normal, as in cases of obesity, and also in morbid conditions associated with imperfect oxidation.

Mucoid metamorphosis sometimes occurs.

Fatty degeneration is seen in severe infections.

Pigmentation is seen in malaria and conditions of marked hemolysis.

False pigments—soot, coal-dust, etc.—are sometimes carried into the bone-marrow by the blood, so forming part of general anthracosis.

Inflammation of the bone-marrow, or *osteomyelitis*, takes place in various of the specific infectious diseases. The more severe grades lead to abscess formation. The process is characterized by the formation of punctiform hemorrhages, focal necroses, cellular infiltration of the walls of the blood vessels, and fatty metamorphosis of the parenchyma, with the liberation of many fatty granules. In the focal lesions red blood corpuscles are absent. The marrow, as a whole, is redder than normal and may be purulent.

The specific *granulomata* and *neoplasms* as they occur in the marrow will be considered together with the Diseases of the Bones.

DISEASES OF THE THYROID GLAND.

The thyroid gland, which in fetal life is a compound tubular gland emptying its secretion into the pharynx through one or more ducts, becomes in the adult a ductless gland composed of a fibrovascular stroma, inclosing rounded spaces either filled with small epithelial cells or lined with cuboid epithelium and containing an accumulation of colloid secretion.

Congenital Malformations.—The gland may be congenitally absent. It may be abnormally large or small or misshapen. Not infrequently scattered islands of thyroid tissue or small accessory glands are found. These are sometimes remotely situated in the deeper parts of the neck or upper part of the chest, are sometimes found higher up, in relation with the tongue, pharynx, larynx, esophagus, etc.

Absence of the thyroid is usually associated with idiocy and cretinism.

Atrophy of the thyroid gland is almost constant in senility. The gland becomes smaller than normal, the acini, instead of being distended with secretion, are shrunken, and are occupied solely by small masses of cells. In some places the entire epithelium of the acini disappears. In addition to the atrophy it is not unusual to find the tissue of the gland indurated and even calcified.

Hypertrophy of the thyroid gland, together with hyperplasia of its interstitial and glandular tissues, forms the chief changes in the interesting affection known as *goiter, struma*, or *bronchocele.* Unfortunately, however, as so often happens, this term has been rather loosely applied clinically to all enlargements of the gland, and so includes at present a variety of pathologic conditions of various and unknown etiology.

Benign Strumæ.—*Hyperemic struma*, or *goiter*, is an enlargement which depends upon dilatation of the blood vessels of the gland. It is unaccompanied by important changes in the parenchyma, and is usually a transitory affection, appearing and disappearing paroxysmally. It is this form of enlargement that characterizes *Grave's disease, Basedow's disease*, or *exophthalmic goiter.* The tumor may be telangiectatic or cavernous. Interstitial hemorrhages frequently occur and are not infrequently followed by necrosis. There is a growing tendency to regard the phenomena of Grave's disease as depending upon morbid conditions of the paratyphoid glands than of the thyroid gland proper.

Hyperplastic or *parenchymatous goiter*, also called *struma hyperplastica follicularis* or *parenchymatosa*, may be congenital or acquired. It depends upon development of the already formed gland by accumulated secretion within its acini, or by extension of the normal alveoli by offshoots, so that the glandular structure becomes hyperplastic without reverting to the embryonal type.

The growth of the gland is sometimes uniform, affecting the entire organ, but more frequently is limited to one or the other lobe or isthmus; or, being irregularly distributed, causes an irregular nodular enlargement. The organ may be several times the normal size, in some cases even attaining the size of a child's head.

Microscopically, the hyperplastic glandular tissue varies in appearance according to its condition. Parts of the tissue that consist of solid substances—that is, small acini full of epithelial cells—present a yellow color, while the areas in which the alveoli are distended with colloid substance are reddish, translucent, and homogeneous. In the same gland both kinds of tissue are often noticed, and great irregularity exists as to the extent of the colloid accumulation in neighboring alveoli, some being distended, others containing only a drop of the secretion.

Fibrous Struma.—It not infrequently happens that the goiter consists chiefly of connective tissue. This may gradually develop by growth of preëxisting connective tissue, or may take place subsequently to the not infrequent interstitial hemorrhages which undergo the usual retrogressive changes and are slowly replaced by hyaline fibrous tissue. Macroscopically the growth is rounded or nodular, hard, firm, and offers resistance to the knife in cutting. The cut surface shows chiefly fibrous tissue, and is frequently calcified (*struma petrificans*), and, according to Forster, sometimes ossified. The tumors at times present a peculiar radiated appearance, as if the fibers extended toward the periphery from some central fibrous nucleus. Hyaline degeneration of both connective tissue and blood vessels is very common in this goiter, and, together with the loss of the epithelium, may transform the tissue into a hyaline spongy mass with rounded cavities filled with clear fluid.

Adenomatous Struma.—This form of goiter is on the border-line between struma and neoplasm. It is correct to describe only those cases as adenoma in which the growth forms a circumscribed mass in, but separate from, the gland. Unfortunately, however, in the thyroid there seems to be no sharp line dividing such circumscribed tumors from peculiar rapid hyperplastic conditions of the parenchyma in which there is a combination of general enlargement, rapid growth of the alveolar structure, and an atypical vascular apparatus.

Cystic or Colloid Goiter.—Cysts are observed in various forms of goiter. Their formation usually depends upon an unnatural accumulation of secretion in groups of alveoli, the walls of which atrophy and disappear, permitting the colloid contents to form a cyst. Such cysts are quite common, and may be numerous in the parenchymatous and adenomatous strumæ. They are usually about the size of a pea, but may be as large as a pigeon's egg, or in exceptional cases as large as a man's fist. The contents much resembles calves'-foot jelly, but may be more fluid or more solid, or may be discolored by bloody extravasations. The colloid substance is slightly yellowish or honey-like; it may be colorless. The cysts may contain a mixture of colloid substance, fat, and lime-salts; pus may be added to their contents.

Inside of the cysts small papillary projections (*proliferous cysts*) occasionally occur; as a rule, however, the cysts have smooth walls.

Cysts also form in the thyroid as the result of blood extravasations and anemic necroses. The walls of these cysts consist of indurated connective tissue, while the contents vary according to the age and changes incident to the tissue destruction.

Myxomatous Goiter.—In the fibrous struma myxomatous degeneration is rather less frequent than hyaline. It is recognized by its usual characteristics.

Malignant strumæ all depend upon malignant tumors of the thyroid gland. The goiter is a growth accompanied by important secondary effects upon the sufferer. These are partly mechanical and partly physiologic. Of the mechanical effects must be mentioned compression and stenosis of the trachea by bilateral enlargements; passive congestion and edema from pressure upon the large veins; irregularities of arterial circulation in the carotid arteries; cardiac, pulmonary, and laryngeal disturbances from pressure upon the vagi, recurrent laryngeal, and sympathetic nerves.

The excessive secretion and absorption or deficiency of the thyroid secretion bring about changes of nutrition and innervation, and may lead to a peculiar systemic affection known as *cachexia strumipriva.*

Etiology.—The cause of goiter is unknown. It seems to be endemic in certain localities, and is much more frequent in high altitudes than in low countries. It is of frequent occurrence in Switzerland, and is said to be more common in Michigan than in any other part of the United States. It probably has no connection with drinking-water, as was once supposed. A few cases may seem to find their origin in arterial or venous hyperemia, as in pregnancy, heart disease, exophthalmic goiter, violent physical exertion, mountaineering, etc.

It is interesting to observe that cretinism and goiter have much in common, and that where the one disease is frequent, the other is almost sure to be found. About 60 per cent. of cretins have congenital goiter. Goiter may occur, however, without cretinism.

That the thyroid exerts a marked influence upon the nutrition of the body is abundantly shown by the results of surgery and experiment. It is found, however, that a small fragment of thyroid tissue is sufficient to prevent the occurrence of the nervous and nutritive disturbances (tetany, epileptiform convulsions, loss of intellectual power, stupor, and cachexia).

When the thyroid is removed or seriously diseased, the hypophysis cerebri usually hypertrophies, as if to carry on a compensatory function.

Amyloid disease of the thyroid gland occurs only in general amyloid disease.

Inflammation (*thyroiditis*) may result from traumatism or infection, and may be mild and of short duration, or suppurative and highly destructive. The abscesses contain a mixture of pus, colloid matter, etc. The termination may be by rupture, with escape of pus into the surrounding tissues, or by encapsulation, gradual absorption, and ultimate calcification of the exudate.

Occasionally thyroid abscesses perforate into the larynx, trachea, esophagus, pleura, mediastinum, etc., in each case followed by subsequent changes peculiar to the affected tissues.

Gangrenous inflammation of the thyroid is sometimes seen in cases of carcinoma with infection.

A mild degree of inflammation also frequently accompanies the infectious diseases, especially typhoid fever. It usually heals by absorption.

The more severe infections sometimes depend upon inflammation of neighboring tissues, as in diphtheria, or upon hematogenous distribution of bacteria, as in pyemia, malignant endocarditis, wound infection, and the like.

Tuberculosis of the thyroid is unusual. It was found by Chiari in 7 per cent. of the cases he studied. Miliary tuberculosis of secondary origin is the usual form.

Syphilis is also rare in the thyroid gland. Demune and Birch-Hirschfeld have described gummatous nodes the size of a pea, usually in the glands of new-born infants and in combination with gummata of other organs.

Actinomycosis has been observed in the thyroid gland.

Parasites.—*Echinococcus cysts* have been observed in the thyroid.

Tumors of the Thyroid Gland.—**Fibroma** in the form of circumscribed nodular growths is easily differentiated from the fibrous struma, and is rare.

Sarcoma is more frequent. Various forms are described—round-cell, spindle-cell, giant-cell, fibrosarcoma, alveolar sarcoma, and angiosarcoma. The round-cell sarcoma is probably most frequent. The tumors usually originate as circumscribed growths, but soon show some disposition to spread. A case which I have examined remained local for five years and was then removed.

It is declared by Wölfler that muscle-fibers may be contained in some of the sarcomata, suggesting that they are of teratoid nature.

Carcinoma is the most frequent primary tumor of the thyroid gland. It is usually soft and medullary, but may be hard, and forms an irregular nodular mass which may be as large as a child's head. It may grow from any part of the gland, and may gradually fade away into normal glandular tissue, or the entire thyroid gland may be transformed into carcinoma. The tumor usually grows from an already existing goiter. Metastasis is not infrequent, and not rarely the disease penetrates neighboring structures, causing carcinomatous infiltrations or becoming infected itself.

Microscopically, the tumor corresponds to the adenocarcinoma, sometimes to the cylindric epithelioma. Squamous epithelioma is mentioned by Ziegler, with the statement that it is very rare.

Colloid changes in the cells of the thyroid carcinoma are very frequent.

Secondary carcinomata are frequently observed in the thyroid when carcinoma of neighboring organs exists.

Adenoma can be recognized as such only when occurring as a circumscribed node, otherwise it is impossible to separate it from the glandular hyperplasia.

DISEASES OF THE HYPOPHYSIS CEREBRI OR PITUITARY BODY.

The hypophysis consists of two lobes: The anterior larger lobe, which is a peculiarly constructed epithelial gland derived in the period of embryonal development from tissues of the digestive tract, resembles the structure of the thyroid slightly; the posterior smaller lobe consists solely of neuroglia, and is derived from the tissue of the middle cerebral vesicle.

Hypertrophy.—Hypertrophy of the pituitary body, by which it attains the size of a pigeon's egg, is infrequent. It may give rise to no symptoms, or may accompany acromegaly, cretinism, myxedema, and other affections. It is said that when the thyroid gland is diseased or excised, the pituitary sometimes enlarges to three times its normal size, as if taking on a vicarious function. The enlarged organ shows an unusual amount of colloid substance in the acini.

Inflammation of the hypophysis is rare. It is usually acute and may be suppurative. It results from inflammations of neighboring parts by extension through the lymphatics. It may also be of hematogenous origin. Chronic inflammation is sometimes associated with thickening of the basilar portion of the dura. In such cases the gland is held in its position in the sella turcica by unusually and abnormally resisting thickened dural tissue. The gland may atrophy or may be abnormally fibrous in consequence.

Tuberculosis and **syphilis** of the hypophysis are rare, and are characterized by the presence of tubercles and gummata.

Tumors.—The most frequent tumor of the hypophysis is the **sarcoma.** It usually forms nodular tumors which sometimes seem to develop from the capsule. The tumors are of mild malignancy, and though they infiltrate and destroy the hypophysis, they rarely infiltrate surrounding tissues and never give metastasis. The tumor may be either round-cell or spindle-cell sarcoma.

Angiosarcoma is occasionally observed.

Adenoma is also a frequent tumor of the hypophysis, and seems to be the growth most frequently associated with acromegaly. It causes a universal enlargement of the hypophysis, with complete atrophy of the posterior lobe, and transforms the gland into a mass of elongate and branched tortuous tubes. It is not easy to differentiate between the adenoma and glandular hypertrophy.

Lipoma of the hypophysis is very rare.

Teratoid tumors are not infrequent.

Cysts of the hypophysis are usually formed by retention of the colloid substance. They occur in the gland and in adenoma. The cysts may become as large as hens' eggs. The hypophysis normally contains a rounded space of small size, lined with ciliated epithelium. This space is most prone to cystic dilatation.

Pathologic enlargements of the pituitary body may occasion blindness by pressure upon the optic tracts and commissure.

DISEASES OF THE ADRENAL BODIES.

Congenital Malformations.—The adrenal bodies are very rarely absent. Occasionally they are abnormally small or abnormally divided, so that fragments of their structure are adherent to or inclosed in the tissue of the kidney (*hypernephroma*) and of the liver; or the fragments are scattered about the neighborhood of the kidney or in the ligaments of the uterus. Instead of scattered fragments, there may be well-formed accessory adrenals. The organs rarely become diseased, though when the disease is marked, interesting pigmentations of the skin may be observed; and it is now accepted that the physiologic office of these organs is to regulate the pigment production of the body.

Degenerations.—**Fatty degeneration** is very common in the adrenal. It gives the gland a lemon-yellow color and softened consistence, and may so alter its structure that the medullary substance seems to melt away and transform the organ into a thin-walled sac. The wall consists of cortical substance infiltrated with fat and partly degenerated. The cavity is lined with soft reddish detritus from cellular destruction. The cause of the condition is unknown. It probably is clinically of little importance, being found very frequently where little suspected. Postmortem changes may contribute to intensify the softening of the medullary substance.

Amyloid disease is known only in the adrenal as a part of general amyloid disease. It attacks the parenchyma very slightly, if at all, but brings about atrophy by pressure. The disease affects the blood vessels and connective-tissue framework, but does not seem to affect the function of the organ even when far advanced.

Pigmentation occurs in senility. It usually affects the deeper cells of the cortex, which appear of a diffuse yellow color from the presence of fine granules.

Hemorrhage of the adrenals is very unusual. It may depend upon circulatory and traumatic causes and may attain considerable size. The blood may be absorbed, may become encysted, or may be followed by induration and calcification.

Inflammation of the adrenal, except the specific infectious varieties, must be very rare. It is probably always of hematogenous origin, and is secondary to other infectious processes. Ziegler speaks of its termination as suppuration and cicatrization.

Syphilis rarely occurs, but usually assumes the form of gumma. Round-cell infiltrations and vascular changes, together with indurations, are also observed.

Tuberculosis is an important and not uncommon disease of the adrenal. In the form of *miliary tuberculosis* it is not infrequent in cases of advanced pulmonary disease. The miliary tubercles are, however, unimportant and small.

Primary caseous tuberculosis of the adrenals is probably the most common lesion associated with Addison's disease.

The organs are enlarged, are surrounded by a thickened capsule, and have an irregular nodular surface. Upon section, the cheesy masses characteristic of tuberculosis are observed. Not only are cheesy masses found, but cavities filled with curdy pus are also frequently seen. Indurations, and in infrequent cases calcified areas, occur.

The lesion may be unilateral, but is usually bilateral. It is not always primary, as cheesy tubercles may occur in pulmonary and intestinal tuberculosis.

Tumors of the Adrenals.—**Sarcoma** occurs not infrequently. The gland may be entirely destroyed.

Adenoma and **carcinoma** also occur. Both sarcoma and carcinoma may be associated with Addison's disease.

Glioma and **neuroma** have been described. Both are rare and rather doubtful tumors.

Secondary sarcoma and *carcinoma* are not uncommon.

CHAPTER VII.

DISEASES OF THE MOTOR APPARATUS.

THE BONES.

While to all appearances the bones remain structurally stationary during the years between adolescence and senility, they are in reality subject to continual alterations in size, strength, shape, density, and composition. The bones of youth contain proportionally more organic and less mineral substance than those of age, and are more resilient; the bones of the period of life's greatest activity are shapely and marked by conspicuous ridges and processes, each of which has some definite anatomic or physiologic reason for its existence, but which at once begins to disappear when activity is diminished. Thus, the alveolar processes of the maxillary bones are especially designed to support the teeth and maintain their integrity while teeth are present, but are soon absorbed and smoothed over when the teeth are lost. The regulation of this formation and destruction of the osseous tissues is naturally subject to some kind of nervous regulation not yet understood, but, so far as can be seen, depends upon the activity of two cells—the *osteoblasts*, or bone-formers, and the *osteoclasts, myeloplaxes*, or bone-destroyers.

The bones are either long, short, or flat. The short bones, the flat bones, and the epiphyseal ends of the long bones consist of spongy tissue, the shafts and surfaces of solid compact structure. They are either of cartilaginous or of membranous origin. The epiphyseal ends originate from separate centers of ossification, and are separated from the shaft by cartilage as long as the bone has not yet attained its full length, the growth of the long bones depending upon this cartilaginous mass. During the growth of the bone the osteoblasts are working away vigorously on the outside to deposit new lamellæ, and the osteoclasts are working with equal vigor on the inner side to destroy and remove the old tissue.

Diseases of the bones may, therefore, depend upon excessive or inadequate growth, excessive destruction, suspension of elongation, failure of the epiphyses to unite, tendency of the epiphyseal cartilages to overgrowth, as well as upon inflammation, infection, specific granuloma, neoplasms, etc. One very important pathologic condition not seen in any other organ is *fracture*, which is very common, especially in the long bones.

Congenital Malformations.—There are no known cases of absence of all the bones. It occasionally happens, however, that certain bones are absent; thus, cases are on record in which there was total absence of both clavicles, of both radii, of both bones of the forearms, etc.

General hypoplasia of all the bones, but chiefly of the long bones of the extremities, is seen in dwarfs (*microsomia*). If the hypoplasia is confined to the limbs alone, the condition is described as *micromelia*; if confined to the cranium, *microcephalia*.

The causes of osseous hypoplasia are summed up by Schmaus to depend upon—(1) Insufficient development of the epiphyseal cartilages in the long bones and of the ossifying connective tissue at the edges of the flat bones; (2) premature ossification of the same tissues, by which subsequent growth is rendered impossible.

Acquired Malformations.—One of the most common causes of acquired malformation of the bone is a peculiar irregularity of structural development known as *rachitis*.

Rachitis (*Rickets*).—Rachitis is a constitutional and nutritional disorder, with osseous lesions characterized by deficient calcification and increased absorption of the bones, which, in consequence, are permanently altered in size and shape. All parts of the skeleton are affected. The bones are usually shortened, thickened, rarefied, curved, and twisted. The rarefied condition is most distinctly seen in the epiphyseal ends of the long bones, which become considerably enlarged.

Etiology.—The disease is not infrequently congenital, and seems, at times, to be hereditary. The exciting cause is unknown, except that it seems to be a frequent result of malnutrition, bad hygiene, and the like. It is most common among the poor, and is very frequent in those countries in which there are many poor. In the congenital form the causes mentioned probably operate upon the child through the mother. The disease affects both sexes alike. When acquired, the disease appears before puberty. It is usually evident in the first or second years of life, but according to some authorities, may be delayed to the tenth year. In cases that live beyond puberty, the disease recovers, but the deformities persist. Dentition is irregular and delayed.

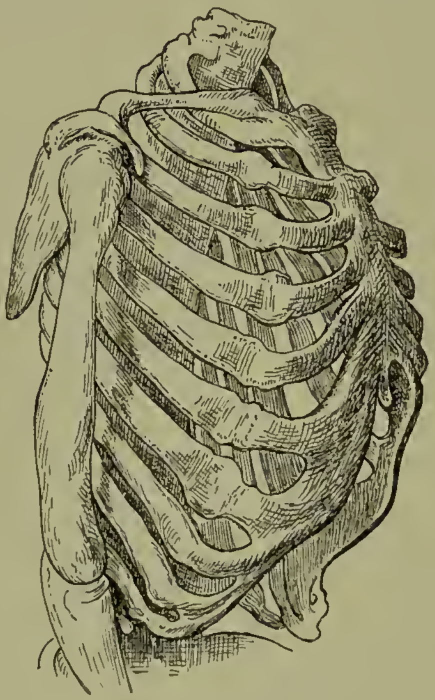

FIG. 290.—Rachitic thorax. The bead-like enlargements at the costochondral junctions are well shown (Orth).

Morbid Anatomy.—The most characteristic deformities produced by rachitis are a peculiar square shape of the head, which is large in proportion to the body. The forehead is high and prominent, and the fontanels long remain unclosed. The anterior fontanel often remains open for four years instead of the normal twenty months. Sometimes there is failure of ossification or perhaps absorption of osseous substance in local areas of the cranium (*craniotabes*). This is seen only in infants. The chest is almost always changed to a "*pigeon-breast*" form with a decided keel in front and transverse grooves on the level of the ensiform cartilage. The end of each rib at the junction with the costal cartilage is enlarged, so that a series of little bead-like growths descend the chest along the costochondral junctions, forming what is sometimes called the *rachitic rosary*. The clavicles may be abnormally curved and thickened at their ends.

The spinal column in rachitis may escape deformity unless the disease is very marked, when lordosis or kyphosis occurs and intensifies the normal curves. The pelvis suffers a deformity well known to the obstetrician as the *rachitic flat pelvis*. The anteroposterior diameter is markedly diminished, and the ilia are separated more widely than normal. The deformity results from a combination of muscular tension and the weight of the body.

The deformity of the long bones varies with the age of the patient, the duration of the disease, and the movements and muscular efforts made. Patients with rachitis usually walk late and hence sit a great deal. The result is that the tibiæ and fibulæ are usually considerably curved, the convexity being outward. The femur, on the other hand, is curved anteriorly and externally. The patient being weak, supports himself in the sitting posture with his hands; hence the humerus and bones of the forearm also become deformed, while probably the greatest enlargement of the epiphyseal unions is observed in the radius and ulna.

The *microscopic appearances* of rickets are quite characteristic, and are best observed at the articular extremities of the long bones, though discoverable in all parts of the skeleton. At the articular end of the bone, where the diaphysis joins the epiphysis, instead of a narrow distinct white line, one finds an enlargement consisting of porous, irregularly formed bone in which there is a widely separated, plexiform or fibrillar arrangement of osteoid substanced eficient in lime-salts. These areas alternate with others of irregular ossification. The marrow is chiefly of the red variety, and resembles that of the fetus. It occupies greatly exaggerated spaces in the rarefied bone. Next to the well-vascularized growing cartilage of the epiphysis there is a zone of osteoid tissue in which the bony partitions inclose cartilaginous islets. This zone may be wide (15 mm.), and is well supplied with vessels. The osteoid partitions have an entirely different appearance from the normal, and between them are accumulations of spindle and irregular cells with occasional round-cells. Farther out the calcification begins, always in the center of the osteoid partitions.

The irregular growth and rarefaction of the bones give them a pronounced predisposition toward bending and fracture, especially of the *green-stick variety*, while the continued pressure exerted by the weight of the body produces permanent deformities.

With increasing years and strength and with improved diet the conditions ameliorate, more bone is calcified, and ultimately the short, thick, curved bones become sufficiently solid to support the body satisfactorily. Their curves and irregularities, however, persist.

Osteomalacia, or **halisteresis**, is an acquired disease of the bones of unknown origin.

Etiology.—It usually affects adult individuals of the female sex, though it is also sometimes seen in males. It is most frequent among the poorer classes, and is sometimes referred to insufficient and vegetable diet. Pregnancy, rheumatism, infection, intoxication, etc., all have been blamed for its development. It is more frequent along the Rhine River and in central Germany than elsewhere.

Morbid Anatomy.—The disease is characterized by a soft, plastic condition of the bones, which depends upon the replacement of the original calcified osseous tissue with a new uncalcified osteoid tissue. It is thought by some that the presence of lactic acid in the blood has something to do with it by aiding solution of the salts, but it cannot be proved.

The disease usually lasts for years, during which time the bones are subject to frequent fracture and increasing deformity, while the patient becomes more and more feeble and adynamic, until a profound cachexia comes on. The patients may die of exhaustion, but much more commonly succumb to pneumonia or some other intercurrent affection.

The bones in osteomalacia, in spite of their limeless character, usually retain their lamellar arrangement, and their external and internal construction are alike histologically unchanged, except that the great mass of the bone is decalcified. The decalcification of the bone usually begins at the periphery and extends toward the center. The altered bone appears homogeneous, sometimes fibrous. The lamellar arrangement may be distinctly visible. Some of the lacunar cells remain after decalcification, but many die. No doubt the persistence of the decalcified bony tissue for a long time in an unaltered condition indicates that it is capable of repair should the prevailing conditions disappear. When, however, the disease goes on progressing, the osteoid substance melts away and increases the spaces between the columns of bony tissue.

At times halisteresis is local, as in the neighborhood of tumors, but, as a rule, it is a wide-spread affection of the entire skeleton. The general disease only is correctly called *osteomalacia*.

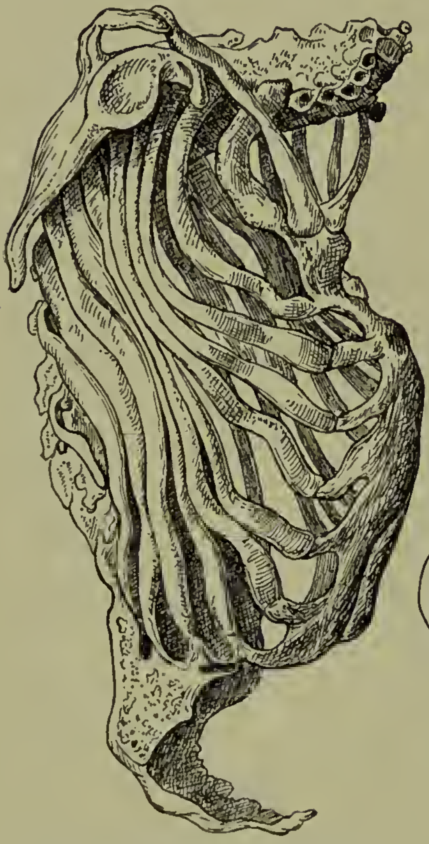

FIG. 291.—Osteomalacic thorax, showing an extreme degree of deformity of the ribs and sternum (Orth).

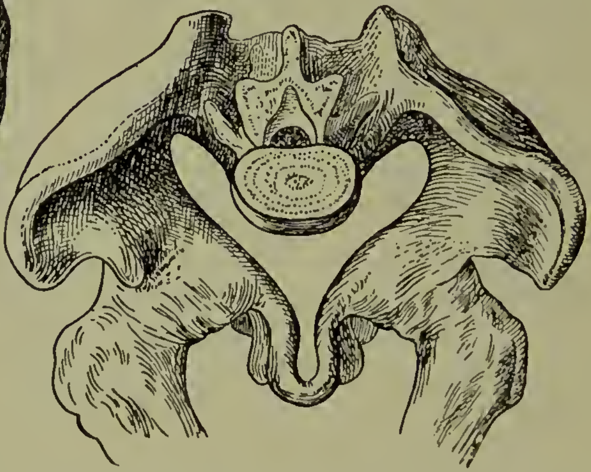

FIG. 292.—Osteomalacic pelvis, showing the diminished capacity of the pelvic cavity and the beak-like projection of the pubes (Orth).

The ordinary form of osteomalacia begins in the spinal column and thorax, and spreads to the bones of the limbs and head.

The marrow of the osteomalacic bones is usually congested, and may be hemorrhagic or pigmented, from previous hemorrhages.

The bones become soft and can easily be broken or cut. Sometimes there is only a rind of osseous tissue surrounding a fully decalcified bone. The bones become curved and shortened. Frequent fractures occur from slight injuries and serve to deform the bone. Kyphosis, lordosis, and scoliosis all occur in the spinal column.

Probably the most interesting and important changes occur in the pelvis, which, being subjected to downward pressure of the spinal column and upward pressure of the thighs, yields, both in its anteroposterior and anterolateral diameters. The first effect of this pressure is the descent of the sacrum toward the pubes and ischii, greatly reducing the anteroposterior diameter; the second, the elevation of the pubes from the pressing of the thighs upward and inward, causing the symphysis and horizontal rami to project anteriorly like a beak, and allowing the acetabula to be brought much nearer together than normal. The deformity transforms the cavity of the pelvis, so that when seen from above, it has somewhat the shape of a three-leafed clover. With a pelvis of this kind child-birth may be impossible.

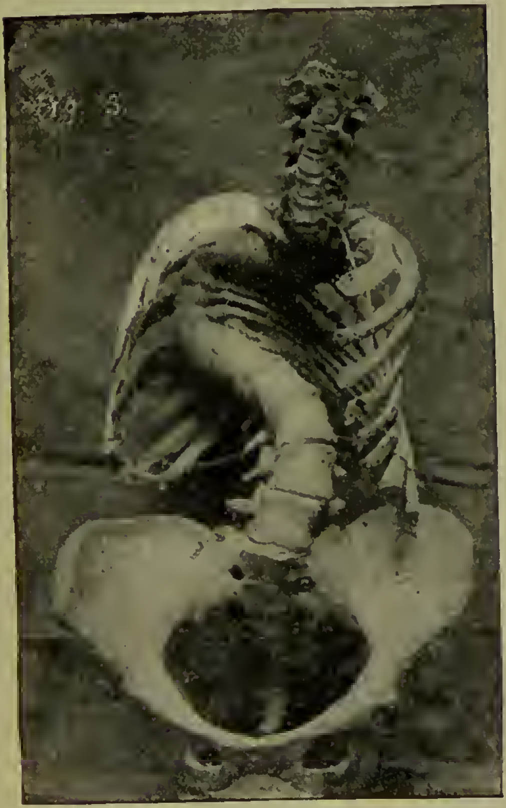

FIG. 293.—Lateral curvature of the spine (scoliosis) (White).

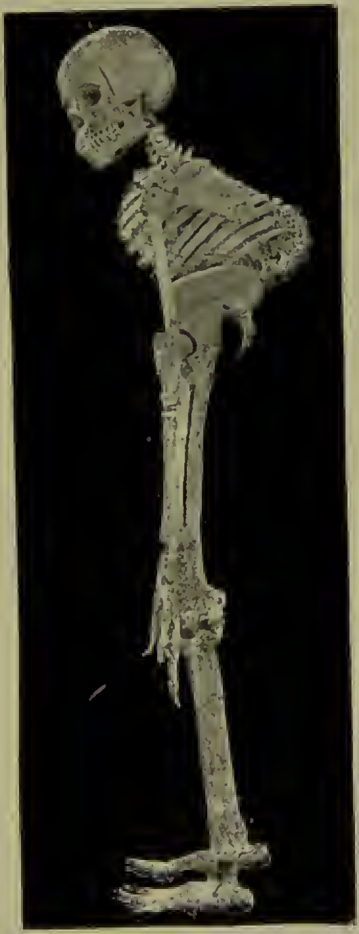

FIG. 294.—Pott's disease of the spine (spondylitis) with kyphosis or posterior curvature (White).

Hyperemia of the bones is characterized by redness of the periosteum, which is also swollen. The spongy substance is brownish or bluish-red in color, and bleeds when cut; the compact substance is slightly reddish.

Thrombosis in the nutrient vessels of the bones occurs in consequence of necrosis and other diseased conditions. The anastomoses are, however, so frequent that no distinct damage results.

Hemorrhage from the periosteal and other vessels occurs in consequence of traumatism, especially fracture of the bones. Small hemorrhages are usually rapidly absorbed, and, unless infected, do little harm. Hemorrhages between bone and periosteum may cause superficial necrosis by dissecting up the membrane.

Caries of the bone with laceration or erosion of the vessels sometimes occurs, but the resulting hemorrhage is unimportant.

Scurvy and infectious and toxic diseases sometimes cause hemorrhages of small size in the medullary substance.

One of the most interesting subperiosteal hemorrhages occurs in the new-born babe, and is known as *cephalohematoma*. It is usually observed upon the parietal bone, and corresponds to the presenting area of the cranial surface that was not pressed upon by the uterine tissues—that is, corresponded to the os. It is seen only in protracted labors. Rarely the condition is double, when one side probably corresponds to the os uteri, the other to an obturator foramen. The pericranium is dissected up for a circle as large as a silver dollar, and forms with the scalp a projecting tumor which always escapes the sutures. The elevated periosteum begins the formation of new bone at its edges, before the blood can be absorbed, so that a bony ring circumscribes the tumor. Ultimately blood and bony ring are alike absorbed. Dangerous and fatal results from suppuration, gangrene, meningitis, and the like occur in cases which, from operation or other causes, become infected.

Atrophy of the bones is a frequent pathologic condition. In the growth of bone the osteoblasts are busy forming new lamina upon the outer surface, while the osteoclasts continually absorb and remove the older internal parts. In atrophy the normal balance of formation and absorption is overthrown, and the bone is destroyed more rapidly than normal. Three varieties are described: *Eccentric atrophy*, which begins within and extends outward. This is the usual form. *Concentric atrophy*, which begins outside and extends inward. *Porous atrophy*, in which, by increase in the size of the Haversian spaces, the bone is made porous. This latter form is often called *osteoporosis*. The increased marrow of the atrophic bones is largely, and sometimes purely, fatty marrow.

Atrophy of the bones of the cranium sometimes takes place without appreciable cause. I have seen a skull from a patient only thirty years of age, in which there was no disploë, and the united inner and outer tables were as thin as paper.

Senile atrophy is observed in the flat bones, especially where no muscles are attached. It is most conspicuous in the skull, where the parietal bones are involved and suffer loss of the external plate and diploë, leaving only the hard internal plate. The atrophic tissue is sunken and marked by distinct demarcations. The jaw-bones also lose their alveolar processes and change their shapes, and nearly all the bones have their angles and edges rounded and often rarefied.

When, in consequence of morbid changes, the bones become extremely brittle, the condition is described as *osteopsathyrosis*, or *fragilitas ossium*.

Atrophy sometimes follows disuse of the bones, as when limbs are amputated and the bones of the stumps are no longer functional, or when limbs have been paralyzed for many years.

Neuropathic atrophy, or atrophy of the bones depending upon nervous disease, may result from trophic disturbances. It is almost indissolubly associated with inactivity of the parts affected. It is seen in cerebral and spinal palsy.

Pressure atrophy of the bones may result from the presence of neoplasms, etc. Pressure atrophy takes place much more readily when nutritive disturbances are already in progress in the osseous tissue. One of the most interesting cases known is that of a cranium in one of the German museums, marked by a deep circular groove where a student's cap had pressed during life. Tumors of the pituitary body frequently cause the bony walls and prominences of the sella turcica to atrophy. It is well known that aortic aneurysms erode—cause to atrophy—the bodies of the vertebræ and other bones upon which they press. All forms of pressure atrophy are local.

In the interior of atrophic bones the softening and liquefaction of the tissues sometimes form *cysts*, with clear fluid, rarely hemorrhagic, contents.

Hypertrophy of the bones is observed in *akromegaly* (*q. v.*). It is less a universal enlargement of the bones, however, than a tendency toward hyperostosis—that is, the formation of periosteal osteophytes which form nodular and acuminate prominences upon the bones and so change and deform them.

The bones of giants are, of course, larger than those of normal-sized persons, and, indeed, in most cases, they are giants because of the excessive length of the bones. Local hypertrophies occur to compensate for unusual strain and permit of firmer muscular attachments.

Partial gigantism affecting fingers or other members is occasionally seen, sometimes occurring symmetrically. The most remarkable form of this bony hypertrophy, or perhaps hyperplasia, is the disease known as *leontiasis ossium.*

Inflammation of the Bones.—Inflammation of the bone may affect the covering osteogenetic membrane and subjacent lamella (*periostitis*), the osseous substance itself (*ostitis*), or the marrow and contiguous bony tissue (*osteomyelitis*). Any of these may occur independently of the others; combinations are frequent; all three may occur together.

Etiology.—The causes of the inflammation are traumatism and infection. Sometimes the traumatism apparently operates without infection. Infection without traumatism depends upon hematogenic metastasis.

Periostitis.—Periostitis is inflammation of the osteogenetic membrane.

Etiology.—It may result from traumatic injuries, especially those associated with an external wound, from the hematogenous distribution of such bacteria as the streptococcus, staphylococcus, typhoid bacillus, etc. It also occurs as a complication of other forms of bone-disease.

Various forms of the disease are described, but are probably only modifications of the same process.

The disease may be *acute* or *chronic.* According to its etiology, it may be divided into *primary* and *metastatic.*

In *acute periostitis* the morbid changes are probably found first in the periosteum itself, which becomes swollen, hyperemic, and when traumatic injuries have been present, more or less infiltrated with blood. In uncomplicated cases the disease may get no further, and terminate by simple resolution, but, as a rule, infection takes place and suppuration occurs. The pus usually collects between the periosteum and the bone, elevating the membrane—*subperiosteal abscess.* This may extend to the adjacent soft parts and produce phlegmonous inflammations, but more frequently by denuding the bone of its life-giving membrane, brings about a molecular destruction of its surface. This causes mineral structure of the bone to crumble away, leaving softened and excavated areas, while particles of the disintegrated osseous tissue lie free as bone-sand in the surrounding tissues. To this molecular death and destruction of bone the name *caries* is given. Sometimes the superficial denudation of bone is so wide-spread and the damage done so great that the superficial lamellæ die—*necrosis*—and slowly detach to form what is called a *sequestrum,* which must be discharged through an external wound before healing can go on.

The infectious process not infrequently ascends the marrow cavity through the orifices of the nutrient vessels, and so produces *secondary osteomyelitis.*

The purulent exudate of periosteal abscesses seems occasionally to undergo a peculiar gelatinous degeneration, by which a tenacious, semifluid substance is formed. This has been described as *albuminous periostitis.*

The acute forms terminate either in recovery without damage to the bone, when the abscesses are absorbed or rupture externally; or in caries or necrosis, with subsequent chronic disturbances induced by the proceeds of bone-destruction, that may continue during the patient's entire life or require surgical interference. The disease may be fatal.

Malignant periostitis is simply a very acute, severe, purulent periostitis, which follows unimportant injuries or arises idiopathically or from pyemic infection.

Chronic periostitis may begin as such or may follow the acute forms. Its occurrence usually suggests prolonged irritation. It is divided into the fibrous and ossifying forms. In *fibrous periostitis* the characteristic feature is the transformation of the periosteum into a dense fibrous tissue, closely adhering to the bone. It is seen sometimes in chronic ostitis and in chronic inflammation of the joints.

Ossifying periostitis is seen sometimes in pregnancy, in tumors, in syphilis, and in tuberculosis of the bones. It is characterized by the formation, beneath the periosteum, of a loose bony tissue consisting of delicate columns of bone with marrow substance between them.

When the bone-formation, instead of being limited to the periosteum, extends to the surrounding connective tissue, it is called *periostitis ossificans.* The change probably begins in detachment of the osteogenetic membrane here and there, then bone-formation from the elevated or detached periosteum, and the subsequent union of the newly formed bone to the underlying bone. The changes may be circumscribed or diffuse. Probably the *hypertrophic osteoarthropathy* seen in the hands, forearms, legs, and feet in chronic tuberculosis of the lungs and emphysema depends upon similar changes.

Ostitis and osteomyelitis are almost indissolubly associated. Ostitis signifies inflammation of the marrow, spongy tissue, and cortical substance of bone; osteomyelitis, inflammation of both bone and marrow. The term osteomyelitis is the better, since it is almost impossible to find the bone inflamed without involvement of the marrow, or the marrow inflamed without the bone being affected.

Osteomyelitis is infectious and at times seems to depend upon micro-organisms, which are disseminated by the blood and lodge in the vessels of the bones. At other times it depends upon direct infection from wounds accidentally or surgically inflicted. Not rarely it depends upon previous periostitis. Staphylococcus pyogenes aureus, Streptococcus pyogenes, the typhoid bacillus, the Bacillus coli communis, the gonococcus, the spirillum of relapsing fever, and numerous other bacteria have been observed in the pus. The disease is apt to follow typhoid fever, scarlatina, small-pox, etc., and is more frequent in young people than in those beyond middle life.

The disease usually begins in the marrow cavity of the long bones, but may occur in the short bones, or even in the flat bones of the skull. The marrow is first found to be deeply congested and of a dark-red color. When the bone is sawn through, the hyperemia of the marrow makes itself evident by a swelling of the marrow, which causes it to bulge outward. Later the hyperemia is the cause of numerous interstitial hemorrhages. In the majority of cases there is more or less suppuration, the pus causing the marrow to become spotted or streaked with grayish-yellow. From the medullary cavity the inflammation may extend to the periosteum, causing inflammation there, and extends from the shaft of the bone into the epiphyses, affecting the spongy substance of the bone. In young persons the inflammation may cause separation of the epiphyses from the shaft and may extend into the joints. The pus frequently collects in small pockets or abscess cavities in the bones. These abscess cavities often unite to form large purulent collections in the bone. In very severe cases wide-spread necrosis may result.

The greater number of cases heal by resolution, some in erosion of the bone, external evacuation of the pus, necrosis, and then a chronic inflammatory process set up by the sequestrum. Some cases are fatal in consequence of pyemia. Amputation and other traumatic forms of ostitis are apt to take on a gangrenous character, the marrow of the bone softening to a discolored, badly smelling mass, and the bone necrosing to a considerable extent. The antiseptic precautions now employed in surgery make *traumatic osteomyelitis* an infrequent affection.

The extent of the necrosis that may follow osteomyelitis and periostitis is variable according to the severity of the case. In very severe cases, in which the periosteum is dissected away from the bone, the entire shaft may die, while in cases limited to small areas comparatively little necrosis will be observed. The dead bone is known as a *sequestrum*, and may occupy a central position—that is, the medullary cavity or a superficial subperiosteal one.

The reaction observed in the bone in close proximity to the diseased areas is interesting. Within the bone, where the effects of the irritation are felt, there frequently develop numerous osteoclasts which invade the bony substance more or less rapidly. Upon the exterior, where the periosteum is stimulated, the osteoblasts become unusually active and form new lamellæ which are not so regularly distributed as normally, but are often deposited in a trabecular form suggestive of periostitis ossificans. In this way the bone becomes irregularly shapen, porous, and thinned. The focus of active inflammation is usually accompanied by more or less marked *caries*, or molecular death of the bone, by which the pus slowly erodes its way to the exterior, rupturing through the soft parts and leaving sinuses communicating with the seat of disease. Such an opening is often described as a *cloaca*, and will not heal if a sequestrum be retained at the seat of disease. As the severity of the inflammation subsides a vigorous new formation of bone is sometimes attempted, but the effect of the sequestrum is always to check the effort. If, by accidental or surgical means, the sequestrum be removed, or if, after the lapse of time, it be absorbed or dissolved, the wound heals kindly, new bone is formed, passes through the regular developmental stages, and is finally finished off to very nearly the original form and appearance.

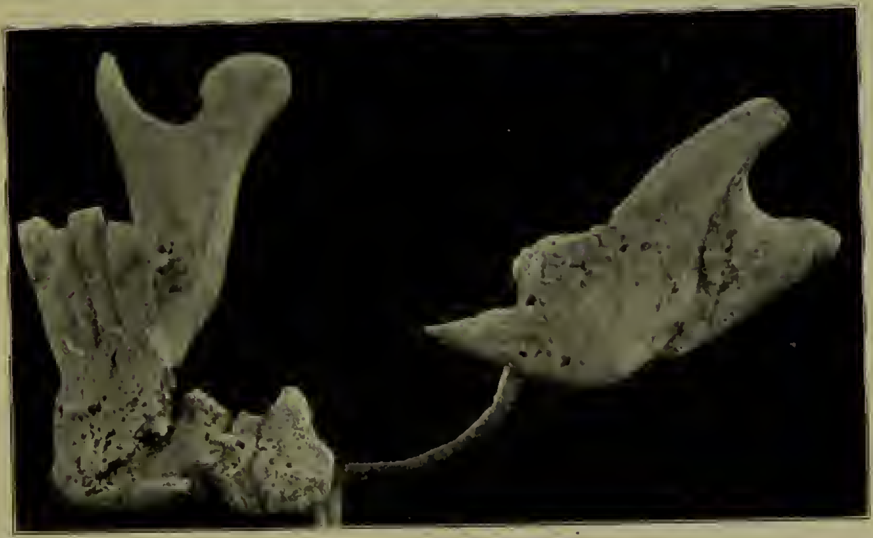

FIG. 295.—Phosphorus-necrosis of the entire lower jaw (Mears).

Chronic osteomyelitis results from the acute osteomyelitis chiefly by the continued irritation of the retained sequestrum. Sufficient has already been said of this form in the preceding paragraph. There are, however, two very important changes which characterize chronic ostitis which are not seen in the acute forms. They are *osteoporosis* and *hyperostosis*. Both of these are seen only in chronic ostitis, because the acute forms are scarcely of long enough duration for their development. The former leads to unusual sponginess of the affected bone, the latter to the formation of bony excrescences or outgrowths.

Phosphorus-necrosis of the bones, which is seen in those who for long periods work in an atmosphere containing phosphorus. The disease seems to result from the entrance of the phosphorus into the mouth, where, because of diseased teeth or gums, it is able to come in direct contact with the bones of the jaw. The disease is peculiar in that it attacks the maxillary bones oftener than any others. It seems to be a question whether or not the disease can occur without the aid of bacteria. In all probability they are always present, and no doubt perform their part in the inflammatory process. The first changes seem to result from sclerosis of the periosteum, which is followed by suppuration, then by caries and necrosis and exfoliation of the necrotic portions. The disease is progressive, extremely destructive, causes wide-spread necrosis with cloaca formation, sinuses, and fistulæ, and may, in rare, very severe cases ultimately bring about complete loss of the inferior maxilla.

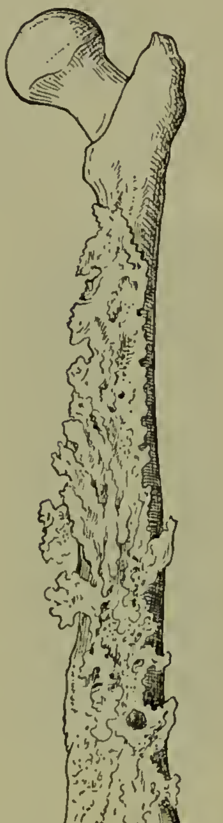

FIG. 296.—Exostoses of femur (Orth).

Ostitis hypertrophicans is seen in acromegaly. It affects the terminal portions of the skeleton in young or middle-aged persons, and is characterized by the formation of periosteal osteophytes, forming irregular rounded and pointed excrescences sometimes closely approximated, sometimes remote from one another on the bones of the hands and feet especially, sometimes the bones of the forearms and lower legs.

Ostitis deformans is a disease of senility characterized by absorption of the bone (*osteoporosis*) and change of shape, resulting chiefly from the effect of pressure. It is sometimes called *rarefying ostitis*, to differentiate it from *sclerotic ostitis* or *osteosclerosis*. The bones affected are chiefly the femur, skull, and spinal column.

The osteoporosis depends upon increased destruction of the bony tissue. It may be observed both in the spongy and compact bone. The condition has already been mentioned under atrophy of the bone.

The type of pressure change that occurs is the commonly observed elongation and descent of the head of the femur at the anatomic neck until it assumes a horizontal position. When the bones become very yielding, the weight of the head often compresses the bodies of the vertebræ more or less, so that the spinal column becomes bent forward to an almost kyphotic condition. The disease is closely related to arthritis deformans and osteomalacia.

One of the important changes observed in bones subjected to inflammation for a length of time is that which is probably analogous to cicatricial formation of the connective tissue and known as *osteosclerosis*. It may occur, without any apparent cause, in senility in the diploë of the skull, causing it to become thick and dense; it sometimes constitutes the process by which rarefied bone is restored to density. Local sclerotic areas in the interior of bones are known as *endostoses*.

Osteosclerosis always occurs about carious and necrotic areas, constituting one of the chief means by which the sequestrum is surrounded by new dense bony tissue. Osteosclerotic exostoses of ivory-like hardness are described as *eburnations*.

Tuberculosis.—This is the most frequent chronic affection of the bones. It usually occurs in youth, frequently in childhood, and is one of the most benign forms of the disease.

The most frequent seats of the disease are the epiphyses of the long bones, the wrist- and ankle-bones, the hip, the spinal column, the ribs, and the phalanges. It may occur from hematogenous metastasis to the bones in tuberculosis of other organs, and not infrequently arises from extension to the bones by continuity of adjoining tuberculous tissue. When the disease is of hematogenous origin, it may occur in the form of minute, disseminated, miliary tubercles as part of general miliary tuberculosis; or it may begin in the interior of the bone in the medullary substance. If it be of periosteal origin by direct extension, it is of superficial occurrence. The disease spreads more rapidly in the spongy tissue than in the denser tissue, and when first observed in the cortical substance, soon extends to the porous parts of the bone. From the bone it is prone to invade the joints.

The disease begins with the formation of the usual miliary tubercles, which are chiefly observed in the marrow or in a newly formed granulation tissue. They extend in all directions by lymphogenic extension, and thus invade the Haversian canals, extending into compact as well as spongy structure. Wherever the tubercles form, the bone suffers from one or another of several complications. Sometimes the inflammatory hyperemia and reaction are sufficient to stimulate the osteoclasts to unusual activity and so absorb the bone in a manner described as *lacunar erosion;* at other times the coagulation necrosis and degeneration bring about caries, there probably being no condition in which caries is so frequent as in tuberculosis of bone. Finally, the formation of tubercles in the Haversian canals sometimes occludes the blood vessels of the bone, and causes an anemic area corresponding to their distributions, in which the bone undergoes necrosis in a more or less well-marked conic area. Together with the carious and necrotic changes which increase the size of the spaces within the bone, granulation tissue, multiplication of tubercles, cheesy degeneration, etc., occur.

The eroding process leads to the formation of a mass of detritus which, when external to the bone or escaping from it through carious openings, infiltrates the soft parts and forms what is clinically known as a *cold abscess.* From the openings in the bone fungous granulations frequently project. The collected products forming the cold abscess do not excite much reactive inflammation in the affected tissues, but gravitate along muscle-sheaths and tendons, often coming to the surface at remote parts of the body, as in the psoas abscess of spinal tuberculosis, or, as it is often called, *Pott's disease.* The erosion of the compact and spongy tissues of the bone, with the openings which sooner or later connect the interior of its marrow cavity with the exterior, cause much deformity; but additional deformity, in the form of thickening and porosity, is brought about by the periosteal changes. The erosion and perforation of the bone are analogous to cavity formation in the lungs. The actually diseased periosteum takes no part in the change, becoming either tuberculous or degenerating; but the periosteum just beyond the invaded tissue being stimulated, shows the changes known as *ossifying periostitis,* with much new-bone-formation by which the bone is greatly thickened and becomes unusually porous. This condition is frequently called *spina ventosa.* The exact extent of the deformity depends upon the size of the osteophytes formed.

After the evacuation of the products of disease tuberculosis of the bones not infrequently recovers, the bone-formation of the periosteum serving to replace much of the lost tissue. The bone, however, often, if not always, remains much deformed. When groups of bones, such as the vertebræ, are affected, the loss of substance is frequently followed by collapse and a general deformity of the body in the form of *kyphosis, lordosis,* etc.

Amyloid disease is apt to form a serious complication of tuberculosis of the bones.

Syphilis of the bones may be of hereditary or acquired origin. When acquired, it constitutes a feature of the tertiary form of the disease. The bone pains and rheumatic symptoms of secondary syphilis are not associated with any definite structural alteration of the bones.

The lesion of **hereditary syphilis** is a peculiar and characteristic *osteochondritis*. It is characterized by an increased width of the zone of calcification between the diaphysis and epiphysis of the long bones, and by a tendency for its tissue to extend irregularly and in a jagged manner into the cartilaginous tissue, and to be here and there interrupted by uncalcified areas. The formation of the marrow cavity is not bounded by a sharply defined straight line, but the ossifying tissue extends irregularly into it. The bony lamellæ of the diaphysis are delicate and insufficiently developed, and the calcifying zone shows a whitish or reddish-white color, and has a peculiar consistence. The newly calcified tissue is porous.

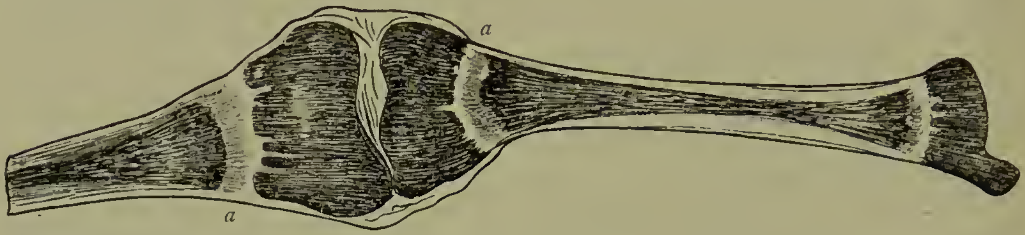

FIG. 297.—Syphilitic osteochondritis: *a*, *a*, Line of cellular infiltration at epiphyseal junction (Orth).

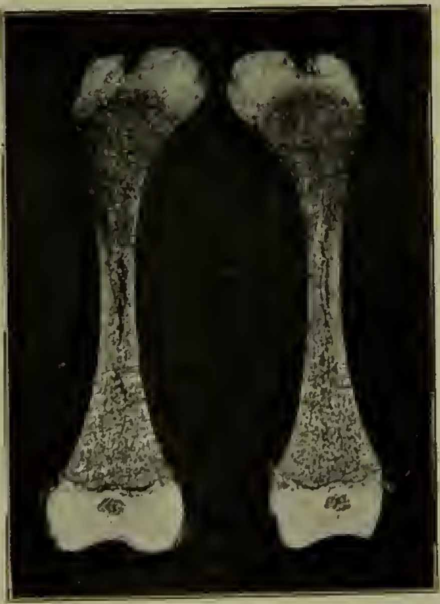

FIG. 298.—Syphilitic osteochondritis; the irregular broad line of ossification is well shown. From an infant which died from congenital syphilis (Hektoen).

In marked degrees of the disease, sometimes designated as a *second stage*, the condition greatly resembles rachitis. Sometimes the tissue is soft and gelatinous. The most marked degree, sometimes called the *third stage*, is characterized by the formation of an irregular layer of well-vascularized granulation tissue between the diaphysis and the cartilage, having a reddish or grayish-yellow color. This sometimes becomes purulent and constitutes the *yellow line*, one of the well-known signs of congenital syphilis. Its ultimate outcome may be the actual spontaneous separation of epiphysis and diaphysis. The point best adapted for the study of this lesion is the lower end of the femur.

Acquired syphilis manifests itself chiefly in the form of gumma, followed by caries and necrosis. It occurs principally in the tertiary stage of the disease, and may be superficial—*syphilitic periostitis*—or deep—*syphilitic osteomyelitis*.

Syphilitic periostitis usually occurs in the periosteum covering the shafts of the long bones. It seems to select by preference those bones which are very superficially situated, as the sternum, scapula, tibia, clavicle, ulna, ribs, and cranium; it may be determined by contusions or other slight injuries of the bone. Next to the bones above enumerated, the phalanges seem to have the preference. It begins in a rather wide-spread cellular infiltration of the deeper structure of the periosteum, and in the formation of an inconsiderably elevated swelling. The cells soon undergo the well-known gummy necrosis. If the cellular infiltration be wide-spread, the necrotic changes may occur in local, scattered areas only. The subjacent bone is eroded, sometimes becomes carious, and often sustains a superficial necrosis. Upon large flat bones, like those of the skull, the changes are more marked than elsewhere. The outer table is first affected and becomes carious; the diploë is next invaded, and the inner table may also suffer. The disease sometimes descends even to the dura mater. The bone is rarely, if ever, uniformly affected, but the disease occurs first in small local areas, which increase in size and number, and often become confluent, so that the entire surface of the bone, or indeed of the whole skull, may show signs of the destructive process. While the disintegration is progressing in parts it is healing elsewhere, so that the nature of the lesions discovered at autopsy is varied.

Syphilitic osteomyelitis is rare in the long bones, and is said to be most frequent in the diploë of the skull and in the phalanges. It is characterized by the formation of single or multiple, large or small, yellowish or grayish, fibrous, gelatinous, or purulent areas, in which, together with the coagulation of the exudate, caries and necrosis of the bone may be observed.

The process of repair in this syphilitic affection of the bones is not long delayed, as a rule, but advances with the extension of the disease. It is most evident at the surface, where osteophytes are produced. The final outcome of the process is usually either *osteoporosis* or *osteosclerosis*, unless death from intercurrent affection takes place. Periostitis ossificans frequently occurs.

The cicatrices which are subsequently observed are rounded, more or less stellate, and are frequently depressed in the center.

Lepra is accompanied by osseous lesions partly dependent upon the leprous lesions themselves, and partly upon local infections resulting from the anesthesia and involuntary injuries likely to be inflicted in consequence. The leprous lesions consist of nodular formations in the marrow and consequent osteomyelitis. The complications are chiefly characterized by necrosis, and not infrequently lead to loss of the phalanges and marked consequent deformity —*lepra mutilans*.

Actinomycosis is not infrequent in the jaw-bones of infected animals. It is chiefly characterized by a suppurative osteomyelitis and ostitis, with more or less caries and necrosis. Upon microscopic examination the ray fungi are likely to be found within the intra-osseous abscesses in the bone.

Tumors of Bone.—The primary tumors of bone are exclusively of the connective-tissue type. Secondary epithelial tumors—carcinoma—are not infrequent. The tumors always originate either from the periosteum or from the marrow, and at once divide themselves into *periosteal* and *myelogenic* forms.

The **periosteal tumors** develop from the osteogenetic layer of the periosteum and lie between the bone and its membrane; more rarely they develop from the periosteum, embracing all its layers. The bone substance is usually embraced in the tumor, but may lie beneath it and escape involvement altogether.

Myelogenic tumors may be circumscribed, but more frequently invade the bone gradually. Their pressure upon the bone, or their extension into it, is likely to produce lacunar atrophy, much resembling halisteresis ossium. As the bone is destroyed, new layers are usually formed by the periosteum, so that unless the tumor grow very rapidly, it remains incased in a well-formed but much distended bony incasement. When the surrounding bone becomes very greatly attenuated, a condition is produced described by the older writers as *spina ventosa*, in which the bone crackles beneath the fingers when crushed.

Osteoma is a tumor in which bony tissue is the chief histologic element. These tumors, having already been discussed, need not be again considered (see Osteoma).

Fibroma usually grows from the periosteum, though it may develop in the marrow. It occurs in the mouth, nose, and pharynx, from the bones of the skull. Occasionally it is seen elsewhere, as upon the buttock and extremities. The tumor is nodular in shape and may be polypoid, especially in the nose and pharynx, and may be telangiectatic.

Chondroma may develop from the periosteum or in the interior of the bones, from cartilage remnants still unossified. They are most frequent in the bones of the hands, feet, and extremities. Sometimes they grow from the cranial bones. They are usually tumors of youth and childhood, and are generally multiple. The *multiple endogenous chondroma* causes the greatest deformity of the parts affected and often renders the individual helpless.

Large chondrous tumors also grow from the scapulæ and from the ribs. They are usually composed of aggregated masses of cartilage, fairly well vascularized, though they frequently undergo softening and may become cystic. It is not unusual for them to attain the size of a man's head.

Myxoma and combinations of myxoma and fibroma also develop from the periosteum. **Lipoma** and **angioma** are rare tumors of the bone.

Sarcoma—osteosarcoma—is the most important and perhaps the most frequent bone tumor, and is the only malignant primary growth. Various forms of sarcoma occur in connection with bone, the spindle-cell and giant-cell forms probably being most frequent. Round-cell sarcoma, angiosarcoma, and pigmented sarcoma occur occasionally.

The *giant-cell sarcoma* is quite frequent as a central tumor of the lower jaw, where it is sometimes described as an *epulis*. It occasionally occurs in the upper jaw, and more rarely at the epiphyses of the long bones. Giant-cell sarcoma may also occur from the periosteum. It is usually single, though it may be multiple.

Spindle-cell sarcoma grows from the periosteum and forms nodular tumors, which may become large. They do not invade the bony substance, as a rule, though they may grow from the marrow substance, when they are much more destructive. *Round-cell sarcoma* usually grows from the medullary substance, rapidly infiltrating and rarefying the bone. As it grows the bone becomes more and more expanded and thinner and thinner, until, sometimes after a great size is attained, the bony capsule ruptures and the tumor invades the soft parts. After the rupture and invasion an ossifying periostitis continues, with the formation of new trabeculæ of bone.

A particular variety of sarcoma of bone is described as *osteoid sarcoma*. It usually develops
upon the ends of the long bones from the periosteum, and is characterized by the formation
of osteoid tissue, and appears to be quite mixed, parts of it being fibrous, parts cellular, and
parts osteoid. There is no regularity as to the amount of bone-formation that can take place,
sometimes a few spicules only being observed, and sometimes dense, ivory-like masses being
formed.

A diffuse form of sarcoma, or at least of sarcoma-like tumors, which affects many bones
and eventually becomes quite general, is that known as *myeloma* or *myelosarcoma* (*q. v.*).
The disease affects the marrow substance and occurs in the form of circumscribed nodes
or diffuse hyperplasia of the marrow. In the neighborhood of the tumor formation the bony tis-
sue atrophies, and it is only rarely that much new bone is formed. The bones usually affected
are the skull, spinal column, pelvis, ribs, etc., which may be filled with larger or smaller
tumors eroding the bone and causing irregularly shaped defects, from which they scarcely
project. The microscopy of the tumors has been considered in the section on Tumors.

Endothelioma, perithelioma, and **angiosarcoma** are occasionally seen growing from the bones of the skull and extremities.

Chloroma, a form of periosteal sarcoma characterized by a greenish or gray color, is occasionally seen.

Carcinoma of bone, as has been said, is always secondary.

Cysts of bones are usually formed by softening.

Parasites of bone are rare. Both the Tænia echinococcus and Cysticercus cellulosæ have been described.

Fracture is solution of the continuity of the osseous tissue. Its most common cause is traumatism, which may act directly, crushing the bone, or indirectly through transmitted leverage. At times fracture may depend upon excessive muscular activity, the strength of the bones being insufficient to sustain strain. Disease predisposes to fracture by changing the composition, structure, shape, and position of the bones. Age predisposes to fracture because of the mineralization of the bones

The bones of adults, for the most part, break with clean edges; those of children, with fibrous connections, causing them to be termed *green-stick fractures.*

Fractures may be single or multiple. A fracture which has a single plane of passage through the bone and divides it into two fragments is called a *simple fracture.* A *comminuted fracture* is one passing through the bone in several planes and dividing in into several fragments. When the fracture communicates with the exterior of the body through a wound of the soft parts, it is called a *compound fracture.* Any fracture in which inflammation, necrosis, or other pathologic change occurs is called a *complicated fracture.*

REGENERATION OF BONE—HEALING OF FRACTURES.

The means by which fractures and wounds of bones recover are easily understood by any one familiar with the developmental stages of bone, and, therefore, needs but superficial description.

The solution of the continuity of the shaft of a long bone is invariably attended by laceration of the periosteum and endosteum, rupture of the blood vessels of the periosteum and often of the bone, and more or less comminution of the soft parts. The immediate result is interstitial hemorrhage, followed by reactive inflammation of the tissue. Leukocytes begin to collect in the suffused area, in which red blood corpuscles and tissue remnants abound in process of destruction. As the detritus becomes more and more broken up the phagocytes scavenge the tissue, removing all the odds and ends of tissue present.

About the second day after the fracture, while the leukocytes are actively at work, the cells of the lacerated and shrěded periosteum and of the neighboring healthy periosteum and endosteum begin to proliferate and form a rather dense tissue, suggestive of the early stages of a cicatrix. Instead of the cells being fibroblasts, however, they are osteoblasts, and instead of a fibrous scar, they form bone. The formation is an osteoid tissue partly formed through intermediate hyaline cartilage, the osteoblasts surrounding themselves with chondrous substance which later calcifies. This osteoid tissue is known clinically as *callus*, or *provisional callus*. It differs from bone in that it is without Haversian systems and is not distinctly laminated. The callus forms in larger or smaller amounts, according to the peculiarities of the individual case, and is evidently nothing more than a temporary framework to support the bone until firm union occurs. Its formation begins as early as the fourth day, and by the end of the first week the bone is quite well supported by it. Surgeons are accustomed to divide the callus into the *ring* and *pin* callus, the former being external to the bone surrounding the seat of fracture; the latter ascending a short distance up and down the medullary cavity of the shaft from the seat of fracture. Technically these are also called *periosteal* and *myelogenic callus* respectively.

Callus is also spoken of as *provisional callus*, which is bone-formation in excess of what will be subsequently needed, and *definitive callus*, which occurs between the ends of the bone, where it must subsequently remain.

Thus far the bony formation about the seat of fracture is a considerable sized, shapeless mass of spongy, atypical, osseous or osteoid tissue, incapable of resistance and forming a very feeble bond of union.

During the period in which the callus has been forming, vessels have been extending into it, exactly as they do in the embryonal bone-formation. The vessels descend into it from the periosteum, from the endosteum, and from the splintered ends of the bones themselves, and until this occurs, the process does not pass beyond the stage of osteoid tissue formation. With the completion of the vascularization the true bone-formation begins by the formation of bony lamellæ about the vessels and the establishment of Haversian systems. In this manner the callus between and immediately about the ends of the bone is transformed into dense, strong bony tissue, which requires weeks for its perfection. The new perfectly formed bone bridges the intervals between the fragments and unites in a common mass any splinters or spicules which have not lost vitality.

The union is now complete, and the bone once more functional. The spindle-shaped enlargement that results, however, is a hindrance to the perfect use of the parts, and, therefore, after a time, absorption begins, and by the activity of osteoclasts through exactly the same method as that seen in the primitive development of bone, the callus is removed after its function has been fulfilled. The absorption process extends over years, and results in the complete removal of all callus, myelogenic and periosteal, in the rounding-off of all angles and corners, and the smoothing of edges and surfaces until, after a few years have elapsed, a well-approximated simple fracture may be so perfectly repaired that it may be almost impossible to determine its exact seat. Such bones, when split by a saw, also show an uninterrupted marrow cavity. The fragments of comminuted fractures may unite with the callus and enter into the bone again, or may be absorbed. If this union be irregular and points or angles project, these are later rounded off.

In the forearms and lower limbs, when both bones are fractured, it is not uncommon for a *synostosis* or union of the four fragments to take place and cause a permanent, though not always troublesome, deformity.

Widely separated ends of bone, bones fractured in the cavity of joints, as the anatomic necks of the femur and humerus, fail to unite. Fractures in badly nourished persons and intracapsular fractures fail to unite because too little callus is formed. Similar failures of union occur at times in marasmus, senility, infectious diseases, etc. When osseous union fails, the ends of the bones may be joined by firm connective tissue—*syndesmosis*—or by loose connective tissue, which permits of motion at the seat of fracture—*pseudarthrosis*. In the latter case, a real new joint—*nearthrosis*—is formed, usually so constituted that one rounded fragment fits into an excavated fragment, the two being surrounded and separated by connective tissue corresponding to a capsular ligament.

The length of time occupied by the healing of fractured bones has been found to be about two weeks for a broken phalanx, three weeks for a broken rib, five weeks for a forearm, six weeks for the upper arm, seven weeks for the tibia, ten weeks for the thigh, and twelve weeks for the neck of the femur. Healing takes place more rapidly in children and in healthy persons than in those advanced in years or weak.

DISEASES OF THE JOINTS.

Fatty degeneration of the cartilage cells is occasionally observed in senility and in inflammatory affections.

Amyloid disease affects the cartilage cells, their capsules, and the matrix of the cartilage, transforming them into amyloid substance.

Mineralization of the cartilages of the joints occurs in senility and gout, or arthritis urica, in which they become infiltrated with salts of uric acid or calcium.

Pigmentation often follows hemorrhage into the joints. The cartilage, capsular ligament, and tendon attachments are sometimes saturated with a brownish or blackish pigment. The condition is sometimes spoken of as *ochronosus*.

Chondromalacia, or softening of cartilage, seems to depend upon loss of the cohesiveness of the fibers of which it is composed, so that the surface frays out and its natural smooth polished appearance changes to velvety. The substance is at the same time softened and often pigmented. Chondromalacia occurs in senile and inflammatory conditions. It may be succeeded by more destructive conditions, such as local erosion, fissures, and cracks, and sometimes cystic colliquation.

Under this head it may be well to mention *abrasion*, *mucous degeneration*, *caries*, and *necrosis*, all of which affect the cartilages of the joints. The necrotic fragments usually develop into true sequestra.

Regeneration of cartilage is seen in fracture, contusion, luxation, and the like. Cartilage heals by the formation of connective-tissue cicatrices. Small fragments, if detached, remain as free bodies in the joints.

Hyperemia of the articular cartilages is seen in traumatic injuries, in mild irritative conditions, and in the beginning of infectious and gouty diseases. The condition first and most plainly manifests itself in the synovial membranes, which are pinkish and injected; next at the edges of the articular cartilages. The amount of synovial fluid is increased and more watery than normal. It is one of the chief characteristics of articular rheumatism.

Hemorrhage into the joints is not infrequent after injury. Small hemorrhages may also occur in inflammation and in the hemorrhagic diatheses. Accumulations of blood in the joint, from whatever cause, are called *hemarthroses*. The condition is unimportant unless accompanied by infection. The blood slowly disintegrates and is absorbed, leaving the tissues more or less deeply pigmented.

Arthritis, or **inflammation of the joints,** is a frequent and important disease. It may depend upon traumatic infectious conditions or upon hematogenous infections in such diseases as scarlatina, pyemia, typhoid, gonorrhea, etc. In some cases the bacterium of the primary disease is the cause of the secondary joint trouble; in others it depends upon complicating organisms that enter accidentally. The disease always first and chiefly affects the synovial membrane, spreading to the cartilages much later. *Synovitis* is limited to the synovial membrane; *panarthritis* affects all the structures of the joint.

Serous arthritis, sometimes also called *hydrarthrosis acutus*, is characterized by serous effusion into the joints. The synovial membrane is congested, swollen, and edematous. Recovery is usually simple and by absorption.

Serofibrinous arthritis resembles the serous form, but is complicated by the presence of fibrin. In some cases the exudation is chiefly fibrinous. As there is much greater difficulty in absorbing fibrin than serum, cases of this variety are prone to run a longer course and be complicated by fibrous adhesions built upon the original fibrinous connections.

A form of serofibrinous arthritis in which the synovial membrane becomes adherent to the articular cartilages and spreads over them like a vascular membrane is sometimes described as *arthritis pannosa* or *synovitis pannosa*.

Purulent arthritis is the most serious form of joint inflammation. It may be limited to the synovial membrane, but is more apt to affect the entire joint. The synovial membrane is red and swollen, covered with fibrin and leukocytes. The joint cavity is filled and more or less distended with pus, and in severe cases the cartilages are softened, eroded, carious, and even necrotic. Perichondritis may occur with peri-articular abscesses.

The acute arthritis may recover by resorption, and even in the extreme form of purulent inflammation may leave no structural changes. On the other hand, even the most simple serous form may become chronic. The serous and serofibrinous forms show changes in the quality of the exudate, which becomes more or less gelatinous or even colloid in appearance. The fibrinous form is accompanied by fibrous adhesions, while the purulent form may invade the cartilages and cause more and more destruction. The essentially chronic forms of arthritis have, however, a quite different etiology, and must be separately considered.

All severe cases of arthritis end in the formation of adhesions, fibrous in ordinary cases, bony in destructive cases. The former inhibits the use of the joint; the latter obliterates it. Either condition is known as *ankylosis;* the former as fibrous, the latter as bony, ankylosis.

Acute polyarthritis, or **acute articular rheumatism,** is an acute febrile disease characterized by painful inflammation of one or many joints. The affection is commonly believed to be infectious, and conflicting results have followed bacteriologic investigation. As a rule, staphylococci have been cultivated from the effusion into the joints, though some observers have discovered bacilli, and others, gonococci. The specific organism has not been determined, and knowledge of the etiology of the disease has thus been retarded. In gonorrhea, metastatic inflammation of the joints—*gonorrheal rheumatism* affecting the knees and ankles—can easily be understood, as there is an active primary disease in progress. The same is true of purulent arthritis following scarlatina and other diseases associated with streptococcic invasion of the body. Rheumatism, however, is often a primary affection, and the avenues by which the infectious agents enter the body are unknown.

The affection not only attacks the joints, but may affect the serous membranes of other parts. Thus, the endocardium is affected in about 25 per cent. of the cases, and the pericardium, myocardium, endarterium, and other serous membranes may be affected. Rheumatism is thus much more than a simple arthritis, as it not only occasions changes in the joints, but also provokes valvular disease in the heart, with many secondary circulatory complications, of which not a few may be fatal.

Morbid Anatomy.—The affected joints are swollen and very painful. They contain an abundant serous exudate in which flakes and shreds of fibrin are suspended or deposited upon the articulating surfaces. The synovial membranes are congested. In cases of considerable duration the cartilages may be eroded, and in chronic cases *fibrous ankylosis* may occur and impede the movements of the parts. The effusion rarely contains many leukocytes, and does not become purulent.

The effusion does not confine itself to the joints, but extends into the periarticular tissue, which swells in consequence. Sometimes it extends into the sheaths of the tendons, these structures at times being first affected.

Recovery may be perfect and without subsequent relapses, but more frequently relapses occur. Not infrequently the disease becomes subacute, affecting joint after joint, and occasioning more or less deformity. The chronic form is followed by ankylosis and deformity somewhat resembling rheumatoid arthritis. The two affections must not be mistaken for one another, however, as rheumatoid arthritis is an insidious, comparatively painless, progressive affection, characterized rather by deformity than by pain; while chronic rheumatism succeeds acute and subacute rheumatism and is characterized by acute attacks of painful inflammatory enlargement of the joints with fever. Rheumatism is commonly followed by endocarditis; rheumatoid arthritis remains local.

Arthritis deformans, or **rheumatoid arthritis,** is a chronic affection of the joints, usually regarded as inflammatory in nature, and by some supposed to depend upon bacteria. The disease is essentially chronic. It is more frequent in advanced years than in youth, but has been observed in childhood. Two forms are described—that affecting single joints (*monarticular*) and that affecting many joints (*polyarticular*). The former is most frequent in the hip- and knee-joints, while the latter usually makes its appearance first in the phalangeal and metacarpophalangeal and metatarsophalangeal articulations. The monarticular form tends to extend to more peripherally lying joints; the polyarticular form to more centrally situated joints.

In the hands the resulting deformity is characterized by a predominance of flexion over extension. The fingers are usually extended, except the last phalangeal joint, which is flexed. As a rule, the wrist is also flexed.

The pathologic alterations are partly degenerative, partly proliferative. The cartilage is softened, fibrillated, and fissured. These lead to considerable destruction of the superficial layer of cartilage, and to excavation of cavities where the proliferated cells degenerate. These retrogressive changes often extend as deeply as the bone. Not infrequently they are accompanied by hyperplastic changes, which form more or less prominent, nodular enlargements at the edges of the cartilages.

As the cartilaginous cellular growths and degenerations descend toward the bone, the tissue often becomes penetrated to a greater or less extent with medullary spaces in which osteoid tissue forms and may calcify.

The tissue of the capsule of the joints also proliferates, the synovial membranes thicken, and often become folded and adherent. Not infrequently the synovial membranes become distinctly villous, and when, as sometimes occurs, fat accumulates in the processes, a peculiar appearance is seen, known as *lipoma arborescens*. Sometimes small cartilaginous and bony growths form in the processes of the synovial membrane, and, becoming detached, form *free bodies* in the joint. The bones also show decided porosity of the articulating ends, in which considerable-sized cavities or cysts may form.

The combined changes of cartilage and bone are succeeded by more or less deformity, which is quite apparent when the skeleton is examined. While occurring in all the affected bones, the lesions are probably most typical in the femur at the hip, and give one the impression that there has been a marked increase of plasticity by which the end of the bone, having been pressed while soft, has run over at the edges while flattening at the surface.

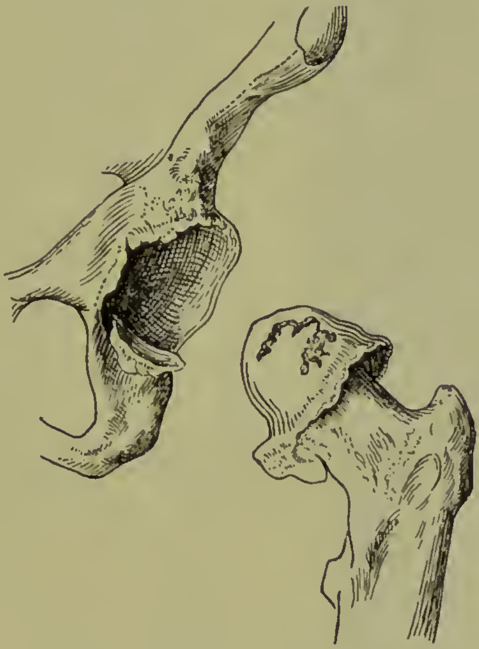

FIG. 299.—Arthritis deformans (Orth).

In this way the flattened head of the bone is surrounded by a rather sharp overhanging bony edge.

If the process be more destructive and the changes extreme, the bone may be so altered in shape by flattening, porosity, excavation, and newly formed processes that it is almost unrecognizable ; indeed, the articular end of the bone may be destroyed or absent. All these changes of the bone take place under the cartilage and are absorptive in nature. This loss of substance must not be mistaken for the result of attrition.

While the destructive process is in progress in the bone, it is usual for fibrous union of the bones—*ankylosis*—to take place, so that the joint cavity is gradually obliterated and the bone immovably fixed. The loss of bony structure often makes necessary a different relation of the ends of the articulating bones, so that a condition of *subluxation* (or partial displacement) is frequent and *true luxation* (or complete displacement) can occur.

The disease is called *spondylitis deformans*, or *rhizomelic spondylosis* when it affects the spinal column.

A form of chronic arthritis resembling rheumatoid arthritis or arthritis deformans sometimes succeeds traumatic or other acute arthritis. It is essentially characterized by vascularization of the cartilage and fibrous union between them. It may affect single joints when succeeding traumatic injuries, or may be common to many joints, as in *polyarthritis rheumatica chronica*, and is called by Ziegler *arthritis chronica adhesiva*. The condition is readily confounded with arthritis deformans, but is differentiated from it by the absence of cartilage proliferation, the absence of superficial cartilaginous destruction, and the simple transformation of the cartilage into fibrillar connective tissue.

Senile arthritis, or **arthritis chronica ulcerosa sicca,** closely resembles rheumatoid arthritis, but is widely distributed over the entire skeleton, thus resembling more closely a nutritional rather than an inflammatory process. The cartilaginous and osseous changes are almost identical with arthritis deformans. The disease occurs in the aged, and most seriously affects the hip, shoulder, and elbow.

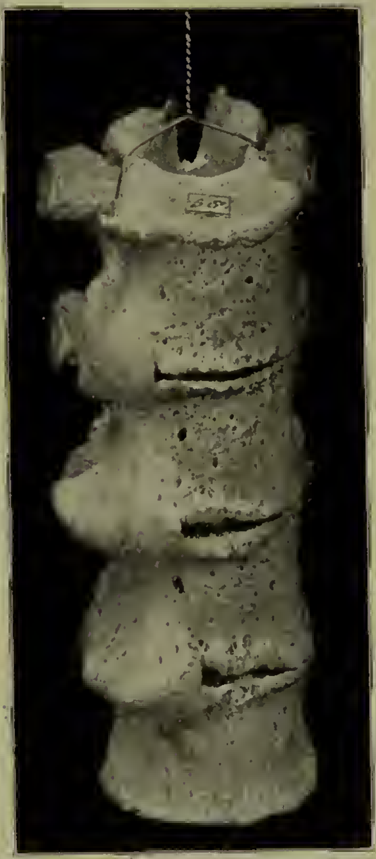

FIG. 300.—Spondylitis deformans. Specimen showing lipping and ossification of ligaments on the right side of the spine (Guy's Hospital Museum).

Neuropathic arthritis, spinal arthropathy, or **Charcot's joint,** is a joint affection observed in posterior sclerosis, syringomyelia, poliomyelitis, transverse myelitis, and a few other forms of spinal disease. It was first carefully studied by Charcot. The joints usually affected are the knee, hip, shoulder, elbow, hand, foot, and more rarely the fingers. The disease is rather rapid and is quite destructive, thickenings and ulcerations forming upon the synovial membrane and ligaments. Serous exudates and inflammations of the peri-articular tissues occur; and spontaneous luxation is not infrequent. The cause of the affection is supposed to be a trophic neurosis. In general the pathologic changes resemble those of arthritis deformans.

Arthritis urica, arthritis uratica, podagra, or **gout,** is a form of arthritis characterized by the deposition of urates in the joints. It is a common affection in England, though more rare in America. It occurs chiefly in persons with a hereditary tendency to what is known as the *uric-acid diathesis*, and is rarely observed except in well-to-do persons, who eat too much and exercise too little. It is sometimes caused by lead-poisoning. This form of arthritis usually affects the smaller joints of the hands and feet, and in the form known as *podagra* is most frequent in the metatarsophalangeal articulation of the great toe. It is a paroxysmal affection, at least in the beginning, and is marked by distinct attacks.

An attack is characterized by redness and swelling of the joint and an effusion into it of clear watery fluid from which salts of the urates are deposited in the matrix of the cartilages, in the ligaments, in the synovial membrane, and sometimes in the neighboring tendon-sheaths. It is an exquisitely painful affection. The salts found in the deposit are urates of sodium, calcium, magnesium, and ammonium; sodium chlorid; carbonate and phosphate of lime, and hippuric acid. They collect in masses, forming at times large, mortar-like or chalky deposits, which are found in the cartilage and ligaments, in the neighboring tendon-sheaths, and in protracted cases in the periosteum and articular ends of the bone. In markedly gouty persons the salts are also deposited here and there in small masses in the subcutaneous tissue, especially in the external ear. Such collections of salts are called *tophi*.

Repeated attacks of the gout are followed by a subacute and finally by chronic arthritis, with softening and fibrillation of the cartilage, erosions upon the surface, proliferation of the periosteum, and more or less periostitis ossificans.

Gout (*q. v.*) is not simply a joint affection of urate deposits, but includes a variety of nutritional disturbances, such as fatty heart, fatty liver, urinary gravel and calculus, contracted kidney, arteriosclerosis, etc.

Tuberculosis of the joints, or **tuberculous arthritis,** is a frequent pathologic condition usually developing in childhood and in those having a hereditary predisposition to the disease. It may affect almost any joint, though those most commonly diseased are the hip, knee, wrist, ankle, spine, and smaller joints of the fingers and toes.

The disease is usually secondary to primary disease of the bones, reaching the articular cartilages by continuity of tissue.

Tuberculosis of the joints is also often of primary occurrence, depending upon the lodgment of tubercle bacilli in the synovial membrane. It seems that in these cases traumatic injuries have some determining importance. They have, of course, nothing to do with the entrance of the tubercle bacillus into the blood, but when they are already present, experiment seems to show that an injury, such as a contusion, may determine that the affected joint shall become the seat of the disease.

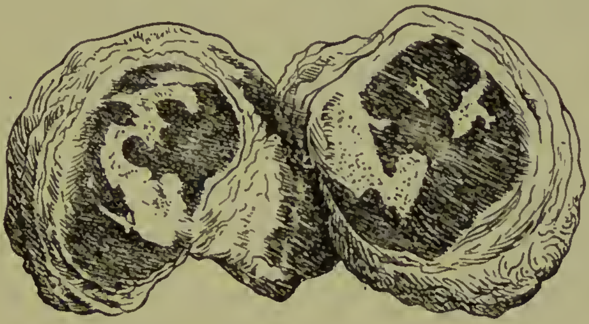

FIG. 301.—Arthritis uratica (Orth).

The tuberculosis usually begins in the synovial membrane, and is characterized by the formation of a rich granulation tissue, projecting on all sides from the membrane, forming a somewhat fungous mass, and justifying the name *fungous joint disease*.

In the granulation tissue many small whitish, yellowish, or grayish tubercles may be found, both by naked-eye and microscopic examination. These tubercles and the granulation tissue in which they occur not infrequently show a pronounced disposition to undergo caseous degeneration. From the synovial membrane the infection extends to the cartilages, this extension not infrequently being preceded by an *arthritis pannosa* which glues the synovial membrane to the cartilages. There are many enlargements at the edges of the synovial fringes, some of them being much like "rice bodies" in appearance. Upon examination they are found to be tuberculous.

When the cartilage is invaded from the bone, the lesions are much more destructive, the invasion being accompanied by more or less wide-spread, superficial or deep erosion, caries, and necrosis. The ligaments of the joint are also affected and often weakened to so marked a degree that subluxations readily occur. As the cartilage and ligaments are eroded, it is not uncommon to find rupture of the joint followed by the escape of a softened, infectious material into the surrounding soft parts. The usual result is *cold abscess.* Such a lesion, especially at the knee-joint, is known as a *white swelling;* at the hip-joint, as *coxalgia.*

According to the course of the disease and the peculiarities it presents tuberculous arthritis is divided into the *fungous form,* in which the synovial membrane develops into a large, spongy, necrotic, or cheesy mass; the *granular form,* characterized by the presence in the synovial membrane of small grayish or whitish tubercles; the *ulcerative form,* accompanied with rapid diffuse caseation, erosion, necrosis, and deformity of the cartilages, invasion of the bones, destruction of the ligaments, and the formation of cold abscess; and the *purulent form,* in which the joint is filled with pus.

Tuberculosis of the joints is usually accompanied by a peculiar swelling of the surrounding soft parts, the skin presenting a white, shining, smooth, bacony appearance, which led the older surgeons to describe it as *white swelling.*

Tuberculous arthritis is characterized by persistent extension with more and more advanced bone and cartilage involvement, and, if the joint be a large one, by ultimate marasmus, amyloid disease, exhaustion, and death. In some cases cold abscesses form, rupture, and leave fistulæ through which the products of disease are eventually discharged. Other cases rupture directly at the surface and permit necrotic cartilage fragments, "rice bodies," products of coagulation necrosis, pus, etc., to escape, so that ultimate healing may go on. Finally, a few cases recover by cessation of the process, absorption of the products, and ultimate cicatrization. It is, however, usual for fibrous adhesions, and, indeed, sometimes dense fibrous or bony ankylosis, to develop. It rarely occasions metastatic tuberculosis of other organs.

Syphilitic arthritis is sometimes observed in children with congenital syphilis. It is a varied process, not well characterized, sometimes manifesting itself in ulcerations of the articular cartilages, fibrous thickenings, and purulent exudate; sometimes as gumma in the tissues of the joint; sometimes in the osteochondritis at the diaphyso-epiphyseal junction.

Syphilitic arthritis of the adult occurs in both the secondary and tertiary manifestations of acquired syphilis. In the *secondary form* it usually appears as serous and serofibrinous inflammations. These may be mild or severe, and sometimes resemble rheumatism. The synovial membrane is usually affected.

The *tertiary manifestations* appear chiefly as arthropathies of chronic course, sometimes resembling arthritis deformans, but differentiated by the stellate and irregular shape of the lesions, and by the fact that they form irregular pits, sharply outlined and surrounded by dense fibrillar cicatricial tissue. These lesions are said to be so numerous at times that scarcely any part of the cartilaginous surface is free and regular. The synovial membrane is usually thickened and adherent. According to Birch-Hirschfeld, these lesions are the result of gummatous disease of the joint.

Tumors of the joints are very rare. The synovial fringes at times become the seat of fatty accumulations and form a variety of lipoma described as *lipoma arborescens* when wide-spread. *Free bodies* or *joint mice* are often formed by hypertrophy of villi of the synovial membrane with cartilage in the interior. These enlarge greatly and are set free by subsequent rupture of their pedicles. These may be as large as a hazelnut, and are most frequent in the knee-joint. Other small bodies—*rice bodies*—are likewise formed from the villi of the synovial membrane, usually during the course of inflammation.

Traumatic Injuries of the Joints.—Luxation.—Luxation is a displacement of the articulating ends of the bones entering into the formation of a joint, with rupture of the ligaments. The immediate effect is the occurrence of some hemorrhage, followed in uncomplicated cases by absorption of the blood and connective-tissue proliferation by which repair is brought about. The changes vary according to the position of the bones. If the bone enters its normal position again,—that is, if the luxation be reduced,—the subsequent changes amount to no more than a *restitutio ad integrum.* If the luxation be not reduced and the displaced bone remains in an abnormal environment, somewhat complicated changes occur. Those tissues pressed upon by the bone atrophy. The articular end, no longer in conjunction with its fellow, becomes covered with connective tissue that chiefly develops from the lacerated capsule. The cartilage becomes fibrillated and gradually changes to connective tissue. New bone is formed, and the condyle of the articulating end becomes diminished in size.

The proximal bone also suffers. If, however, the two bones come together in an unusual position, either they unite by ankylosis or a new joint is formed. This is accomplished through the excavation of the bone by pressure atrophy, and partly by a surrounding bony reinforcement caused by ossifying periostitis. The surrounding connective tissue forms the analogue of the capsular ligament. A synovial membrane finally develops, and a true *nearthrosis* results.

Ankylosis is the union of articulating bones by fibrous or bony connections by which their mobility is partially or completely destroyed. It is a frequent outcome of diseases of the joints, and has already frequently been mentioned. Under such conditions it is usually *fibrous ankylosis*, though *bony ankylosis* may also occur. In cases of surgical resection of bones bony union is always expected. The formation of bony union in these cases is almost identical with the healing of fractures, except that no provisional callus is formed.

DISEASED CONDITIONS OF THE TENDONS AND BURSAE.

Tendosynovitis, or inflammation of the sheaths of the tendons, is a frequent affection. It may be characterized by a serous, serofibrinous, purely fibrinous, or in secondary cases depending upon infected wounds, by a purulent exudate. The disease is painful, and when the parts are moved, a distinct crepitation may be felt, depending upon the movement of the exudate-covered tendon through the exudate-covered sheath. This, of course, occurs only in the form with simple fibrinous exudate, and is often described as *tendovaginitis sicca*.

The disease may terminate by resolution or become chronic.

Chronic tendosynovitis may lead to the formation of dropsical accumulations in the sheaths—*hydrops tendovaginalis;* or, if adhesions form here and there, the dropsy will occur locally in the form of cystic dilatations. From the villi of the serous membrane small bodies similar to those sometimes seen in the joints are formed. They are called *corpora oryzoidea*.

In severe cases the chronic tendosynovitis may lead to strong permanent adhesions between tendon and sheath, and interfere with motion. Hard, rounded cysts of the tendon-sheaths, usually observed upon the backs of the hands and wrists, are called *ganglia*. Their formation depends upon local dropsy and hernia of the sheath.

Tuberculosis of the tendon-sheaths accompanies tuberculosis of the bones and joints. It may occur in the form of diffuse miliary tubercles along the tendon-sheaths, or as caseous masses more distinctly localized.

Bursitis, or inflammation of the bursæ, is seen occasionally, the most familiar form being the *housemaid's knee*, which affects the patellar bursa. The inflammation usually results from traumatic injuries, and may be characterized by serous, serofibrinous, or more rarely purulent exudates. The bursæ may greatly enlarge during the process of disease. Ordinarily the exudate is absorbed. The affection may become chronic, and the walls of the bursa may thicken and show papillary growths from the interior.

DISEASES OF THE VOLUNTARY MUSCLES.

Necrosis of muscular tissue results from traumatic injuries, burns, frost-bite, decubitus, local anemia, inflammation, and a variety of other local causes. It also occurs frequently in the specific infectious diseases, probably most frequently in typhoid fever and diphtheria. The muscle becomes discolored, black-brown or blackish-gray, and melts away.

Hyaline or **waxy degeneration** of the muscle is characterized by indefiniteness and final loss of the transverse striations, and the transformation of the muscle tissue into fragments of shining, hyaline, or homogeneous material which contract within the sarcolemma so that it becomes unusually distinct. Further retrogression of the tissue changes the hyaline bodies into granular masses, sometimes spoken of as *sarcolytes*, which gradually melt away and are absorbed. Hyaline degeneration occurs in the infective diseases, and will be best observed in the abdominal muscles and long muscles of the thigh.

Degenerations of the Muscular Tissue.—*Cloudy swelling* of the muscles takes place under the same conditions as cloudy swelling generally—that is, infectious and toxic conditions. It is characterized by a hypergranular condition of the sarcoplasm and readily passes into fatty degeneration.

Fatty metamorphosis of the muscles succeeds the cloudy swelling in violent irritative conditions, such as phosphorus and arsenic poisoning. The fatty granules are observed in the muscle-fibers, to which they sometimes impart a yellowish color. The knife may become oily when the muscles are incised.

Fatty infiltration of the muscles, or *lipomatosis muscularis*, is a fatty deposit in the muscle *between* its fibers. It is sometimes seen in obesity, but more frequently in the muscular dystrophies, notably the pseudohypertrophic muscular palsy. The presence of the fat gives the muscular tissues a yellow color and a pallor quite unnatural to them. The muscular tissue atrophies in consequence of the pressure of the fatty globules.

Amyloid disease is rare in the striated muscles, though not infrequent in the unstriped muscles. It has been observed in the tongue and muscles of the larynx in a nodular form.

Calcification of the muscles is observed in myositis ossificans (*q. v.*).

Hydropic or *vacuolar degeneration* of the muscles is characterized by the formation of clear drops, single or in considerable numbers, in the interior of the fibers. The condition may be so marked that the fibers appear broken up or even frothy from their presence.

Hypertrophy of the muscles is usually the result of excessive function, and is compensatory. It is best illustrated in the muscles of athletes during training, and in blacksmiths.

Pseudomuscular hypertrophy is a dystrophy, and will be described below. Thomsen's disease is said by Erb and others to be associated with local hypertrophies of the muscles.

Atrophy of the Muscles.—*Simple atrophy* of the muscle-fibers is characterized in a diminution in the quantity of muscular substance in a fiber without appreciable qualitative alteration or structural change. The atrophy may progress to the complete extinction of the fiber, its striæ remaining to the last. The condition occurs in marasmus, anemia, inactivity palsy, and in the neighborhood of tumors. It also occurs in senility.

Brown atrophy of the voluntary muscles is characterized by minute pigment-granules in the fibers, which become darker in color because of their presence. The process is analogous to brown atrophy of the heart muscle (*q. v.*). Brown atrophy of the muscles is not uncommon in senility.

Dystrophy is a term used to express atrophic and degenerative conditions of the muscles in which, in addition to the simple atrophy of some of the fibers, others show dichotomous branchings, splitting, fractures, and vacuolation. Some of the more healthy fibers are hypertrophied. Proliferation of the muscle nuclei and increase of sarcoplasm also occur, and regenerative efforts are probably manifested by the presence of multicellular myoblasts and rows of muscle nuclei between the remaining muscle-fibers. Fatty infiltration occurs between the degenerating fibers in the pseudohypertrophic muscular palsy.

In progressive muscular atrophy the perimysium interium is richer in nuclei and better developed than in healthy muscle, and not infrequently shows fatty degeneration. The greater the loss of muscular tissue, the richer the tissue becomes in nuclear, fibrillar connective tissue, with which the sarcolemma sheath unites. The fibers in process of atrophy usually begin by longitudinal rather than transverse cleavage.

A peculiar form of muscle destruction seen in progressive muscular atrophy is described by Friedreich as *elementary cleavage*, and by Zenker as *discoidal destruction*. It is the splitting-up of the fibers into their contractile discs, depending upon a more rapid destruction of the *kitt-substance* (cementing substance) than of the prisms.

Hyaline degeneration is also sometimes observed in the dystrophies.

The muscular dystrophies are, for the most part, necrotic or neuropathic lesions, seen in diseases of the nervous system, especially those lesions of the spinal cord in which the ganglionic cells of the anterior cornua are affected.

Among the conditions in which they occur may be mentioned—(1) Degenerations of the peripheral nerves, such as occur in the infections and intoxications. This form may recover by regeneration of the muscular tissue after the neuritis recovers. (2) Diseases of the spinal cord, among which may be mentioned myelitis, poliomyelitis anterior acuta, poliomyelitis chronica, or progressive muscular atrophy, amyotrophic lateral sclerosis, and various local lesions of the cord and its membranes. (3) Diseases of the anterior nerve-roots. (4) Diseases of the pons, the progressive glosso-labiopharyngolaryngeal palsy. (5) Diseased conditions seeming to reside in the muscles themselves, and possibly in the nerve-endings, as in pseudo-hypertrophic muscular palsy.

The dystrophies sometimes affect the muscles in groups corresponding to the nerves or nerve-centers affected, sometimes progress fiber by fiber, beginning in certain groups of muscles in a manner not easily explained. Thus the anterior poliomyelitis produces dystrophies of the muscles of the upper extremity when in the cervical region, of the lower limb if in the lumbar enlargement. Progressive muscular atrophy usually begins in the muscles of the hand, shoulder, and buttock. Pseudohypertrophic muscular palsy first shows itself in the calves of the legs, upper arms, thighs, forearms, and deltoids, and gradually spreads.

The dystrophies are, for the most part, progressive, of insidious onset, and slow course. They may terminate in almost complete loss of muscular substance. Few are known to recover.

Myositis, or **inflammation of the muscle,** usually occurs in consequence of inflammation of surrounding tissues. It is frequent in traumatic and infectious wounds and in fracture of bones, and is often secondary to inflammatory diseases of the bones and joints. It may depend upon the presence of parasites, as in the case of trichinæ, and is sometimes occasioned by the hematogenous distribution of bacteria in pyemia. A special form of myositis of infectious origin, affecting many muscles simultaneously, is called *polymyositis*.

The inflammation may be of all grades of severity, but is usually mild. The affected tissue is congested, swollen, and more or less edematous from the presence of a serohemorrhagic exudate. In scorbutus a serohemorrhagic inflammation with considerable bloody exudate is common.

Purulent myositis, representing more serious damage to the tissue, is characterized by abscess formation with necrosis and wide-spread destruction of muscular tissue.

The inflammatory affections of the muscles usually heal readily by absorption of the exudate and regeneration of the lost tissue. or in cases where this is not possible, by the formation of cicatrices which form dense callous connective-tissue masses, and not infrequently lead to deformity by shortening the muscles as they contract. Abscesses sometimes become encapsulated and may become calcified.

Chronic myositis, or **myositis fibrosa,** often follows the acute myositis. It is characterized by connective-tissue formation in the muscle and atrophy of the original tissue by its pressure. It sometimes succeeds neuropathic muscular lesions.

Myositis ossificans is a chronic inflammatory disease of the muscles, succeeding frequently repeated mild traumatic injuries in which bone is formed in the intermuscular connective tissue, fascia, tendons, and aponeuroses.

The bone usually occurs in the form of spicules and plates, more rarely in rings. The disease affects the deltoid, pectoral, and adductor muscles of the thigh, and is seen chiefly in soldiers. The traumata predisposing to bone-formation are supposed to be the frictions and slight injuries caused by the gun and saddle in drilling and riding, whence the names by which the Germans denominate them—*Reit* and *Exercier-Knochen* (riding and drilling bones). The bony formations are not only seen in soldiers, but also among various tradesmen whose muscles are similarly influenced.

Myositis ossificans progressiva is a different affection of unknown origin, usually affecting youthful persons, and beginning in the muscles of the back of the neck, gradually spreading to a great number of muscles, in all of which bony formations occur.

The disease is said to begin in a doughy swelling of the muscle, which is followed by the formation of connective tissue and by some atrophy of the proper muscular substance. In this newly formed connective tissue, as well as in the perimysium, septa, tendons, and aponeuroses, bony formations occur in the form of spicules, plates, bands, cylinders, crescents, etc. There are also frequent exostoses from the bones themselves, especially those of the spinal column.

The outcome of the interesting process is what the museums describe as a *petrified man,* for little by little the bony formation increases until the contractile muscles are replaced by rigid bone tissue, which prevents, to a greater or less extent, mobility of the limbs. The bone-formation may take place directly in the connective tissue, or may occur through the intermediate formation of hyaline cartilage.

Tuberculosis of the muscular tissue is unusual. It is almost always secondary to tuberculosis of the bones and joints, and leads to the formation of either cheesy masses or fibrous indurations. Cold abscesses not infrequently form when tuberculous disease of the bones is associated with secondary disease of the muscles, the cheesy pus finding its way by gravitation to the opposite end of the affected muscle, where the abscess may point.

Hematogenous tuberculosis is rare. It usually assumes the form of miliary tuberculosis.

Syphilis of the muscles is rare, occurring in the form of gumma or of dense connective-tissue callosities. The muscles affected are chiefly those of the upper extremity, especially the biceps, those of the neck, tongue, back, and the sphincter ani. The indurations are associated with atrophy of the muscular tissue.

Glanders and **actinomycosis** occasionally invade the muscles, producing their respective characteristic lesions.

Tumors of the muscles more frequently develop from the septa and fascia than from the muscular tissue itself. Among those described are *fibroma, lipoma, myxoma, chondroma, hemangioma,* and *lymphangioma. Rhabdomyoma* has been observed only in very few cases. *Sarcoma* and its various combinations are occasionally seen forming nodes of various sizes.

Secondary tumors are not infrequent. Of these, *carcinoma* is the most common. It occurs secondarily to carcinoma of the mamma, stomach, epithelioma of the lip, skin, etc., and is sometimes of lymphatic origin, sometimes of hematogenous origin. Carcinoma of the muscles usually assumes the form of a diffuse infiltration, with occasional nodular formations. The carcinoma cells can sometimes be observed in the sarcolemma sheaths, where their pressure upon the contractile substance of the muscle causes atrophic areas which Ziegler compares to Howship's lacunæ of bone.

Secondary sarcoma of metastatic origin is seen occasionally.

Parasites of muscle are numerous. The most important are the *Trichina spiralis*, the *Cysticercus cellulosæ*, and the *Tænia echinococcus*, all of which are described in the section upon Parasites.

CHAPTER VIII.

THE NERVOUS SYSTEM.

DISEASES OF THE SPINAL CORD.

CONGENITAL malformations of the spinal cord are of rare occurrence. Monsters having four legs, two heads, etc., may have double or bifurcated cords, peculiar to the individual case. Sometimes the cord is abnormally long, descending to the sacrum.

Micromyelia is a condition in which the spinal cord is either abnormally short or abnormally small.

Diastematomyelia is a partial doubling of the spinal cord in the lumbar region. Rarely the lower part of the cord is divided at the lumbar enlargement, without coincident division of the spinal column. Sometimes there is a bony septum between the two cords. Each half is typical in its construction and arrangement as regards white and gray matter.

Asymmetry of the cord is sometimes seen. Whole tracts may be missing on one side or on both. The absence of these tracts usually depends upon incomplete development or upon irregular division of the nerve-bundles. The condition may also depend upon irregular pyramidal decussation, by which, in the change to the opposite side, nearly the whole pyramid, instead of one-half of its fibers, cross over.

Heterotopia, or abnormal shape and position of the gray matter, is sometimes seen. The heterotopic appearance may occur in any part of the cord, and may not involve the entire cord.

Heterotopia is closely simulated by artefacts brought about by accidents to the spinal cord in removing it from its bony encasement.

Hydromyelia, or **hydrorrachis**, is a dilatation of the central canal of the cord by accumulated cerebrospinal fluid. It is a frequent congenital condition, related to hydrocephalus interna. The central canal is not only sometimes abnormally large, but in imperfectly formed conditions may be double or seemingly double. The dilatation of the cord in hydromyelia is not uniform, but frequently subject to greater, indeed, almost cystic, enlargement here and there. When hemorrhage occurs into the dilated part, the condition is described as *hematomyelia*.

Amyelia, or absence of the spinal cord, occurs only in brainless monsters (*anencephalia*).

Hydrorrhachis externa is a collection of fluid in the subarachnoid spaces. It corresponds to hydrocephalus externa.

Spina bifida is an interesting congenital condition of not infrequent occurrence. It depends upon incomplete development of the vertebral column, by which the posterior processes, failing to unite, leave fissures or clefts, usually in the lumbar or sacral regions, though occasionally in the dorsal or cervical regions. The clefts are known as *rachischisis*. The spina bifida is formed by a hernial protrusion of the membranes of the cord through this opening. The hernia may be covered with skin, which is usually hairy, or may occur through the skin, leaving the pia of the cord, thickened by external contacts and covered with granulations, the only covering. If the hernial protrusion embraces the spinal membranes only, it is called a *meningocele*. When there is a simultaneous collection of fluid in the interior of the cord, dilating and attenuating it so that it forms a thin layer or sac of the spina bifida, the condition is described as *myelomeningocele*.

Atrophy of the spinal cord occurs in extreme old age, as the result of disease of certain of its structures, after amputation of one of the limbs, and rarely under circumstances which cannot well be explained. In atrophy both the nerve-cells and fibers may be involved, becoming smaller and finally disappearing.

The most important atrophic changes of the cord occur in the anterior cornua of the gray matter, and are characterized by progressive diminution of the ganglion-cells. The condition may progress to complete loss of the cells and a majority of the fibers.

In some cases the atrophy is accompanied by such cellular changes as pigmentation, hyaline degeneration, fatty metamorphosis, and calcification of the elements.

Myelitis is a term used to describe retrogressive changes in the nervous tissue resulting from inflammation and injury. The peculiarities of the nervous tissue are such that it is with much difficulty—if, indeed, it be at all possible—that changes depending upon inflammation can clearly be separated from those resulting from other injurious agencies, such as pressure, intoxication, anemia, fever, etc. By common consent the attempt to do this has been abandoned, and it is now usual to describe the changes found in myelitis simply as degenerative, except in the occasional rare instances of actual suppuration, tuberculosis, etc.

The **degenerations** of the spinal cord may be *primary* and *secondary*. *Primary degeneration* occurs at the seat of original damage, and may be a local circumscribed process. *Secondary degeneration* depends upon primary degeneration elsewhere, and results from the destruction of nerve-cells or axis-cylinders, the distal extensions of which, being cut off from their vital sustaining centers, slowly degenerate. Secondary degeneration may be much more extensive, inasmuch as a primary degeneration involving a short segment of the cord may be followed by a secondary degeneration which will ascend or descend in certain tracts throughout the entire length of the cord.

The degenerations are classified according to the color of the diseased tissue as *white softening*, *red softening*, and *yellow softening*. The differences between these are mere histologic accidents, which will explain themselves in the description of the lesions.

To the naked eye, in the early stages of myelitis, the affected tissue has a swollen, pinkish color, and projects in a convex form from a transverse incision. There may be minute punctate hemorrhages in the tissue. When, instead of involving the entire cord, as in transverse myelitis, certain columns only are affected, they usually become conspicuous by a pinkish-red color in the early stages, by a grayish color in the later stages, and by pigmentation when the lesion is very old. The degenerated tissue may be softened in the beginning of the retrogressive process, but becomes firmer and firmer with the duration of the case, sclerotic changes occurring.

Microscopically the degenerative inflammation is characterized by readily appreciable changes. The myelin of the nerve-sheaths is early destroyed, and becomes transformed into peculiar, irregular, nodose cylinders. These give way to a separation of the myelin in the form of irregular drops, which give the osmic acid reaction for fat. Later these myelin blocks break down into molecular matter. The axis-cylinders become greatly swollen, and usually do not long survive destruction of the myelin-sheaths. The nerve-cells lose the regular arrangement of Nissl's granules, their nuclei become enlarged and vacuolated and later disappear; fatty degeneration of the protoplasm takes place, hyaline degeneration of various of the tissue elements and a more or less complete disorganization of the tissue result. There is no discoloration of the tissue, hence the process is described as *white softening*.

Through such degenerated areas some few nerves may pass without complete destruction, though they usually show the peculiar varicosities of medullary fragmentation.

When the disease occurs in consequence of hematogenous micro-organismal infection, or when, from any other causes, the tissue is infiltrated by leukocytes, these latter are found scattered through the destroyed tissue.

In cases of marked injury to the cord blood sometimes infiltrates the injured tissue, coloring it red (*red softening*). The destruction of the blood and liberation of its pigment in the form of yellowish granules cause *yellow softening*.

In cases of leukocytic infiltration there are usually many more cells in the perivascular lymphatic spaces surrounding the blood vessels than distributed throughout the tissue. These being ameboid and loading themselves with fatty granules and granules of hematogenous pigment, thus scavenge the tissues. Not all these cells are leukocytes, however, some being derived from the endothelium of the vessels and lymph-spaces and from the pia.

Though ganglionic cells sometimes withstand degeneration longer than the elements surrounding them, they sooner or later yield, and the degeneration may be so extensive and wide-spread that only the resistant connective-tissue septa of the cord remain uninjured. The softened tissue also contains more fluid than normal; whether this is a form of edema or whether it results from colliquation necrosis is not clear. Probably the latter is the more correct view.

Corpora amylacea, small, rounded, homogeneous, concentrically laminated bodies, are often seen in degenerated areas. They are thought by some to be formed of axis-cylinders in a state of swelling; by others, to be degenerated cells.

Calcification of ganglionic cells is sometimes, but rarely, observed in myelitis.

Perfect recovery does not occur after degeneration of the spinal cord, the structures being so highly specialized and complexly developed as to make it impossible. Partial recovery and repair is, however, seen in nearly all cases. The fragments of degenerated tissue are slowly dissolved or are removed by the scavenger cells. The leukocytes that have escaped from the blood vessels return again by the lymphatics, or are destroyed and dissolved, and the process of repair begins by growth of the glia and connective tissues. In some of the lower animals the axis-cylinders of nerves still connected with their controlling ganglion cells grow and extend through the regenerating tissue. It is, however, very doubtful whether any such efforts at reëstablishing conduction occur in the cord of man. Should such efforts be made, they are abortive and conduction is not reëstablished.

The stage of regeneration with proliferation of neuroglia and connective tissue is the beginning of what is known as *sclerosis*. The proliferation of glia cells seems to occur most extensively in case the degenerative changes have been limited to the nervous elements of the cord, though it can occur where there has been complete destruction of all the elements.

The newly constructed glia tissue sometimes forms a dense, fine, fibrillar tissue, sometimes a loose network. The fibrillæ represent the branched processes of the neuroglia cells. It seems likely that the formation of the neuroglia tissue is slow.

The sclerotic tissue is usually gray in color, firm, dense, and dry. When the tissue is loose in structure, it may appear gelatinous.

Fibroconnective tissue is not formed in the spinal cord, except in severe lesions associated with laceration, section, suppuration, etc. It develops from the pia mater, from the septa, and from the perivascular connective tissue, and has the ordinary appearances and characteristics of cicatricial tissue.

Both primary and secondary degenerations may begin by affecting an entire tract of the cord from end to end. This is, however, not always the case with primary degeneration; it may be quite local. The secondary degeneration simultaneously affects all parts of the affected tracts, and according to Stroebe, is recognizable microscopically on the second day by changes in the mark substance of the nerves. Destruction of the axis-cylinders follows in a few days. In a brief time the scavenger cells are at work, and absorption of the destroyed tissue is in progress. The result is the formation of soft juicy tissue in which the neuroglia gradually grows, not perfecting its dense fibrillar appearance for months or even years.

Sections through the tissue of the cord will vary in structure at different periods of development. Thus, after two or three months, the cord is composed of a reticulated framework the meshes of which are either filled with fluid or contain scavenger cells with fatty or pigment-granules. Here and there one finds groups of nerve-fibers which may have escaped destruction. In from six to twelve months the reticulated tissue is found to be much denser, and is present in greatly increased amounts. Scavenger cells with contained granules are still present in the various spaces of the tissue. As the sclerotic process advances the color of the diseased tissue becomes gray and its bulk diminishes.

Etiology.—Myelitis may be traumatic, infectious, toxic, or nutritional in origin.

Traumatic myelitis, usually transverse, depends upon injury or local disease of the spinal column. In most cases it is slow, from the increasing compression of the cord, such as occurs in tumors of the cord, tumors of the meninges, and collections of fluid in the spinal canal. The results of such local lesions are manifested upon the entire structure of the cord at the altitude of the lesion, thus giving it the name *transverse myelitis*. If the disease be of sudden formation and attended with simultaneous injury of the blood vessels, the changes may conform to the description of red or yellow softening, according as the cord is studied soon or long after the development of the condition. If the injury be slower, white softening is usually observed.

Infectious myelitis, or *hematogenous myelitis*, is observed in the infectious diseases—rheumatism, typhoid fever, small-pox, diphtheria, pyemia, anthrax, syphilis, etc. Sometimes it results from the dissemination of bacteria through the blood and their colonization in the cord, sometimes from the dissemination of their toxic products. Under these circumstances both transverse and disseminated myelitis may occur, according to the conditions arising.

The anatomic and histologic alterations are identical with those of other forms of myelitis, plus the presence of the bacteria. The disseminated form of myelitis is particularly characteristic of the infectious diseases, and is probably more often caused by syphilis than by other diseases. In syphilis, however, the vascular changes which interfere with local nutrition may have more influence than either the bacteria or their toxins.

Toxic myelitis may depend upon the toxins of the infectious diseases or upon other poisons, such as ergotin, carbonic-acid gas, tetanus, arsenic, mercury, strychnin, etc.

Nutritional myelitis is observed in certain constitutional diseases, such as diabetes, Addison's disease, pernicious anemia, etc.

It is also said that myelitis may follow exposure to cold, excessive fatigue, and sexual excesses.

Varieties of Myelitis.—When the spinal membranes are inflamed, the condition is known as *spinal meningitis;* if the membranes and cord are both affected, as *meningomyelitis*.. Inflammation of the cord alone is known as *myelitis*. Disease of the white substance is called *leukomyelitis;* disease of the gray matter, *poliomyelitis*.

According to its distribution, myelitis is said to be *central* when arising from disease of the central canal; *diffuse*, if it affects the whole cord; *transverse*, if the entire cord is affected for a short distance; or *disseminated*, if it occurs in numerous small areas remote from each other.

Pathologic myelitis is divided into the *simple*, *hemorrhagic*, and *purulent*, according to the condition in which the tissue is found.

Clinically myelitis is divided into *acute* and *chronic* forms. The acute form is of abrupt onset; the chronic form, of insidious onset. Both forms are of indefinite duration, in which sense all forms are chronic.

Termination of Myelitis.—The outcome of all forms is a hyperplasia of the neuroglia tissue, with a resulting gray sclerosis. No regeneration of any importance takes place, although the presence of nerve-fibers in the spinal membranes in old cases of transverse myelitis are taken by some to indicate that an attempt at regeneration is in progress, and these newly formed fibers are seeking an external path in which to pass the seat of disease.

Hydromyelia is a dilatation of the central canal of the spinal cord caused by the pressure of an increased amount of cerebrospinal fluid. The enlargement of the canal may be visible to the microscope only, or it may be widely dilated. Its shape is usually regular, and the dilatation uniform, though it may be greater at certain heights than at others, especially great in the lumbar cord. In some cases the canal is not round, but is slit-like, triangular, or irregular in shape. It is usually lined with ependymal cells of cuboidal shape. In rare cases the canal is double or triple for its entire or for part of its length, the reduplication being more frequent in the lumbar region than elsewhere. Occasionally diverticula extend from the canal into the substance of the cord.

The dilated canal is filled with cerebrospinal fluid. It may, however, contain blood (*hematomyelia*), or in rare cases pus (*pyomyelia*).

Etiology.—The cause of hydromyelia is not always clear. Some cases are congenital. The acquired cases may depend upon abnormalities of blood and lymph circulations, inflammatory changes in the central canal, and degenerative changes in its wall. The condition is not always easily differentiated from syringomyelia, the chief difference being the presence in hydromyelia of the ependymal cells.

The condition, so far as is known, is without clinical significance.

Syringomyelia is an affection somewhat similar to hydromyelia, characterized by the formation of a central dilatation of the spinal canal, in consequence of the degeneration of an abnormal growth of glia tissue in that situation.

The cause of the disease is unknown: it may be the result of developmental errors. It is characterized primarily by a gliosis about the central canal of the cord, especially posteriorly in the neighborhood of the gray commissure, probably beginning in the cervical cord. The extent of the gliosis is unlimited, and it may continue along the entire length of the cord. Secondarily, the disease is characterized by degeneration and liquefaction of the hyperplastic glia tissue. The outcome of the process is the formation of the cavity, which is situated posteriorly to the center of the cord, is of varying size—sometimes a mere canal, sometimes a cavity so large as to distend the substance of the cord, press upon its tissues, and cause them to atrophy and degenerate, giving the impression that the surrounding thin wall can scarcely contain any nervous tissue. When the disease does not involve the entire length of the cord, posterior degeneration higher up is usually present.

The cavity is usually filled with clear fluid, but in cases not quite so far advanced in the process of degeneration this cavity may contain a brownish, gelatinous mass, consisting of the products of tissue disintegration and blood corpuscles; or it may contain blood. It is surrounded by glia tissue.

In some cases the syringomyelic cavity becomes cystic in appearance through the union of cavities in the cord formed by local areas of myelitic degeneration. In fact, some cases of syringomyelia, known as *secondary* or *atypical*, are formed entirely by the union of myelitic cavities or cysts about which gliosis occurs in the process of partial recovery. Such myelitic degeneration is seen in cases of meningomyelitis, in traumatic and infectious myelitis, and in other cases, especially when associated with hemorrhage.

The spinal canal in syringomyelia is usually irregular. and is not lined with ependymal epithelium. It may be centrally situated, but is very frequently asymmetric and often is entirely on one side. When the cavity is large and full of fluid, the cord, which may not have appeared abnormal before incision, collapses as the contents escape and appears flattened and like a ribbon.

The extent of secondary degeneration in the spinal cord and in the anterior and posterior nerve-roots will depend entirely upon the size of the lesion and the pressure it causes. In marked cases whole columns of the cord and anterior and posterior nerve-roots may be destroyed.

Tuberculosis of the Spinal Cord.—The most frequent tuberculous affection of the spinal cord is that which attacks the meninges and extends from them into its nervous tissues (*tuberculous meningomyelitis*). The tubercles, at first small, increase in size and number, and, aided by accompanying round-cell infiltrations, eventually cause considerable thickening and necrosis. From the pia the tubercles gradually invade the nervous tissue, leading to degeneration.

Primary tuberculosis sometimes originates in the cord itself, forming single, circumscribed, cheesy, sometimes softened masses, which may become as large as hazelnuts. Secondary degenerations of the cord are frequent results of tuberculous inflammation and the destruction of the nervous tissue it causes.

Disseminated miliary tubercles of hematogenous origin are also frequent. They occur in both gray and white matter, and can be discovered only upon microscopic examination. The tubercles are typical in appearance, and are frequently accompanied by perivascular infiltrations of small round-cells in the immediate neighborhood. These miliary tubercles, small as they are, may be the origin of secondary degenerations.

Tuberculous spinal meningitis may be limited to the spinal cord, or may affect the cord simultaneously with the membranes of the brain. It may affect either the dura or the pia mater.

Tuberculosis of the dura is most frequent as a result of tuberculosis of the vertebral column. It may be confined to the dura mater only—*tuberculous pachymeningitis*—or may extend from it to the pia and arachnoid. The disease may be *external*, the tubercles appearing upon the external surface of the dura, as when the disease is secondary to vertebral tuberculosis; or *internal*, the tubercles appearing upon the inner surface. In both forms the lesion consists of disseminated or confluent miliary tubercles with cheesy degeneration and the formation of a granulation tissue sometimes replete with tubercles, more or less in coagulation necrosis, and forming accumulations that may compress the cord.

Tuberculosis of the Pia or Tuberculous Leptomeningitis.—This very often results from inward extension of the pachymeningitis. There may be typical miliary tubercles, but there is more frequently an additional inflammation with a suppurative tendency, surrounding the affected area with creamy pus or with a seropurulent exudate. The tubercles are usually distributed along the blood vessels, and may occasion small hemorrhages. The disease may spread to the nerve-roots, and may cause secondary degeneration of the cord.

Syphilis of the spinal cord usually assumes the form of a syphilitic myelitis characterized by degenerations, of which those of the posterior columns are probably most frequent and most important. These degenerations may be in part dependent upon syphilitic disease of the vessels of the cord. with consequent degeneration. There are no characteristics by which the degenerative conditions of syphilis can be differentiated from other spinal degenerations, though posterior and disseminated scleroses are particularly suspicious.

Syphilis of the Spinal Meninges.—*Syphilitic pachymeningitis* may occur primarily or secondarily. Secondarily it occurs through the extension of syphilitic disease from the pia or the vertebra to the dura. As usual with syphilitic disease, the outcome of the process is the formation of dense scars, thickenings, and adhesions of the various parts.

Syphilitic leptomeningitis is infrequent. It is usually characterized by the formation of round-cell infiltrations, forming flattened, extensive swellings. The disease sometimes invades the dura and sometimes affects the subjacent cord. Thickenings, adhesions, and dense scar formations result, which, when they embrace nerve-roots or outlying nerves, lead to their destruction. The degeneration of considerable invaded tissue leads to the formation of cheesy centers in the diseased areas. When the disease invades the vessels of the cord or descends into its substance, degenerations occur and *syphilitic meningomyelitis* results.

Birch-Hirschfeld mentions a *gummatous spinal leptomeningitis* which occasionally occurs simultaneously with a similar disease of the membranes of the brain. When fresh, the lesion is characterized by grayish, gelatinous thickenings.

Lepra of the spinal cord occasionally occurs. The lesion may be recognizable only with the microscope, and is chiefly characterized by atrophy of the ganglionic cells. Rarely there may be areas of softening, occasional interstitial hemorrhages, and inflammatory reactions.

Lepra bacilli have been found by numerous observers in the tissues of the spinal cord. They have been seen in the connective tissue of the cord, both in white and gray substance. When in the ganglionic cells, as sometimes happens, they cause vacuolation and ultimate destruction.

Tumors of the Spinal Cord.—Tumors of the spinal cord are of rare occurrence. Probably the most frequent is the **glioma,** which has already been spoken of in connection with syringomyelia (*q. v.*). Its usual occurrence is in the form of *gliosis* or development along a considerable length of the cord, about or posterior to the central canal. Its growth is accompanied by a simultaneous degeneration which leads to the excavation characteristic of syringomyelia. It is rare that a circumscribed form of glioma occurs. Those seen are usually markedly telangiectatic.

Sarcoma of the spinal cord is very rare. Spindle-cell sarcoma has, however, been seen. **Cylindroma** has also been described.

Gliosarcoma and **gliomyxoma** are uncertain tumors of which a few occurrences are reported. They resemble glioma in general characteristics and distribution, and probably are simply variations.

Fibroma occurs very rarely in the form of rounded, circumscribed tumors. These are apt by pressure to excite degeneration in the columns of the cord. This secondary degeneration applies to all tumors in which local damage is done to the spinal cord.

Tumors of the spinal meninges are much more frequent in occurrence than those of the substance of the cord. They occur in all the membranes.

Tumors of the Pia Mater and Arachnoid.—In fibrous deposits of the arachnoid the deposition of calcareous matter is of frequent occurrence. Whether or not this bears any relation to osteoma is uncertain. *Osteoma* in the form of small, flattened, whitish plaques occurs infrequently in the arachnoid.

Cartilaginous plates also occur in the arachnoid, and sometimes are sufficiently large to be called *chondroma.*

Angioma of the cavernous type sometimes develops from the vessels of the pia. It forms a flat growth, more or less distinctly circumscribed, red in color, and soft in consistence.

Psammoma, sarcoma, myxoma, lipoma, myoma, and *fibroma* are all occasionally seen. Some of these are easily recognizable; others require microscopic examination. The shape is always more or less flattened in order to accommodate them to the canal in which they occur. They all cause more or less pressure upon the cord and are likely to lead to degeneration of its columns.

The sarcomata may be of any variety, but endothelioma is most frequent.

Cylindroma and *cholesteatoma* are of rare occurrence.

Secondary tumors, either sarcoma or carcinoma, are of occasional occurrence in the spinal meninges.

Tumors of the dura mater are probably less frequent than in the deeper membranes. Those most frequently observed are *sarcoma*, *psammoma*, *myxoma*, *fibroma*, *chondroma*, and *lipoma*. A melanotic tumor has also been seen by Williams.

Parasites of the Spinal Cord and its Membranes.—Parasites are very rare in the spinal cord and in its membranes. The *Cysticercus cellulosæ* has been found in the interior of the dural sac in a few rare instances. The *Tænia echinococcus* is perhaps a little more frequent, thirteen cases having been collected by Neisser. Very few of the cases were primary, the greater number having occurred by secondary extension to the spinal canal from contiguous organs, muscles, and bones primarily affected.

Spinal Meningitis.—Pachymeningitis.—Acute inflammation of the dura mater spinalis is most frequently occasioned by inflammations in neighboring tissues or by traumatic agencies. As an idiopathic affection it is of doubtful occurrence. The lesion is characterized by the formation of an exudate, which usually collects upon the external surface (*external pachymeningitis*). It may be cellular or fibrinous. In the former case actual abscess formation is not rare, and may compress or destroy the subjacent spinal cord. In all severe inflammations the term external pachymeningitis is inappropriate, as the condition affects the entire thickness of the dura mater and causes the accumulation of serum, pus, or other exudate, both within and without the dural sac.

Internal pachymeningitis, usually also further denominated *hypertrophica* or *adhesiva*, sometimes results from tuberculous or syphilitic disease and from disease of the pia mater and the bones. The idiopathic occurrence of the affection is not well understood. It is characterized by the formation of a fibrous exudate irregularly distributed, and leading to adhesions between the dura and deeper membranes, or to the formation of a membranous deposit, well vascularized, upon the inner surface of the dura. Small hemorrhages also occur in this newly formed tissue.

Hemorrhagic pachymeningitis may be a modified or exaggerated form of the hypertrophic internal spinal meningitis. It is analogous to the cerebral hemorrhagic pachymeningitis (*q. v.*), and is characterized by the formation upon the inner surface of the dura of a delicately vascularized membrane having a rust brown color, due to frequent hemorrhages. Like the cerebral pachymeningitis (*q. v.*), it is most frequent in the insane, in drunkards, etc.

Chronic hypertrophic cervical pachymeningitis has been described by Charcot. As the name indicates, the disease affects the cervical cord, is chronic, and is characterized by the formation of extensive fibroid thickenings of the dura, pia, and arachnoid. The outcome of the disease is compression of the roots of the nerves, atrophy of the fibers, and degenerations in the cord—transverse myelitis and descending degeneration.

Leptomeningitis.—Acute inflammation of the pia mater and arachnoid results from hematogenous distribution of bacteria, especially in the epidemic infectious form known as *epidemic cerebrospinal meningitis* (*q. v.*). It is also the result of infection from local trauma, disease of the bones, etc.

The lesions characteristic of the infection include the formation of an inflammatory exudate that collects in the meshes of the arachnoid and in the space between arachnoid and dura. The exudation may be serous, fibrinous, or purulent. It may be found upon a limited extent of the membranes when the disease is local; or may, as is more frequent, be found upon the entire length of the cord. To the naked eye the exudate is whitish or creamy in color and creamy in consistence. It rarely happens that the cord entirely escapes, and small round-cell infiltrations usually occur in the anterior commissure and scattered throughout the perivascular connective tissue.

Bacteriologic examination reveals the presence of various bacteria in different cases. In epidemic cerebrospinal meningitis the Meningococcus or Diplococcus intracellularis of Weichselbaum is almost invariably found. It is supposed to be the cause. In other cases the Streptococcus pyogenes and pneumococcus are the most frequently encountered organisms.

The inflammation is liable to affect at least the superficial elements of the cord, so that in all severe cases it assumes the form of *meningomyelitis*. The affected superficial nerve-fibers of the cord degenerate, as do those acted upon by inflammatory extensions that descend into the cord along the vessels and endoneurium.

Circulatory Disturbances of the Spinal Cord.—**Anemia,** or more correctly **ischemia,** usually occurs in the lumbar cord. The pressure of morbid growths and inflammatory collections upon the vessels of the cord, as well as arteriosclerotic conditions in vessels, the thrombosis of the smaller arteries, and embolism of the nutrient vessels all lead to ischemia. Embolism is nearly always followed by anemic necrosis, as the vessels are all end arteries.

Anemia, especially pernicious anemia, may also lead to degenerative changes, especially of the posterior columns of the cord.

Hyperemia.—As dead bodies usually lie upon the back, hypostasis of blood into the vessels of the spinal cord nearly always occurs, and at autopsy must be differentiated from true *antemortem congestion*.

Hyperemia is common in all cases of inflammation of the meninges and in local areas of the cord. Passive congestion occurs in chronic cardiac and pulmonary affections.

Active hyperemia gives the white substance a rosy hue, and causes the gray substance to appear brownish. There may be small punctate hemorrhages into the substance of the cord and into its membranes.

Passive hyperemia is characterized by dilatation and tortuosity of the vessels, a grayish-yellow color of the white substance, and a dark grayish-red color of the gray substance.

Hemorrhage into the spinal cord is much less frequent than hemorrhage into the brain. Punctate capillary hemorrhages and massive hemorrhages are occasionally observed. The punctate capillary hemorrhages appear upon transverse section of the cord as fine reddish dots that cannot be washed away. They occur into the perivascular spaces, and are found after traumatic injuries of the cord, in degenerated areas, in the neighborhood of tumors, in tetanus, in general passive congestion, and in a variety of other pathologic conditions. The blood damages the nervous substance by compressing and disorganizing it.

Massive hemorrhages occur from rupture of blood vessels from any cause, and form collections which rarely exceed the size of a hazelnut. Sometimes the hemorrhagic collections are round, and extend for a considerable distance along the cord between the longitudinal fibers; at other times they make their way into the central canal, rupturing externally into the pia. If the patient live, the changes that occur in the hemorrhagic area are identical with those of hemorrhages into the brain (*q. v.*)

SPECIAL DISEASES OF THE SPINAL CORD.

Disseminated or Multiple Sclerosis.—Disseminated or multiple sclerosis is common to both brain and spinal cord. It is characterized by numerous, rather small, irregularly distributed areas of softening or sclerosis. The disease seems to attack the white matter by preference, but also occurs in the gray substance. It is sometimes apparent that the degeneration has begun in the distribution of a blood vessel or round about it. The lesions, when fresh, are of a grayish or pinkish-gray color, and gelatinous in consistence. When the tissue is examined microscopically, it is usual to find abundant myelin and fatty drops, fatty degenerated cells, and molecular débris. There is nearly always a marked proliferation of the glia-cells, though this develops later. Hyaline degeneration of the blood vessels is usually found, and corpora amylacea are common. This form or stage of the multiple sclerosis Ziegler calls *multiple myelitis*. An interesting feature of the histology of the affection seems to be the retention, despite the softening, of a considerable degree of vitality of the nervous tissue. Thus, while there is destruction of the sheaths of the nerves, liberation of myelin substance, and fatty metamorphosis of the cells, numerous axis-cylinders continue to escape complete destruction and pass through the diseased area still able to conduct some impulses. Birch-Hirschfeld, Schmaus, and others think it is the persistence of these axis-cylinders that prevents the occurrence of secondary degeneration in multiple sclerosis.

As the disease becomes more advanced, the softening gives place to sclerosis, sometimes beginning insidiously. The sclerosis depends upon active growth of the glia tissue. The cells are numerous, the fibers coarse, and the meshes unusually loose. The nerve-fibers in the sclerotic area are atrophic, denuded where there had been previous softening, and some of them disappear. Nerve-cells atrophy. The vessels are abnormally numerous or may be absent.

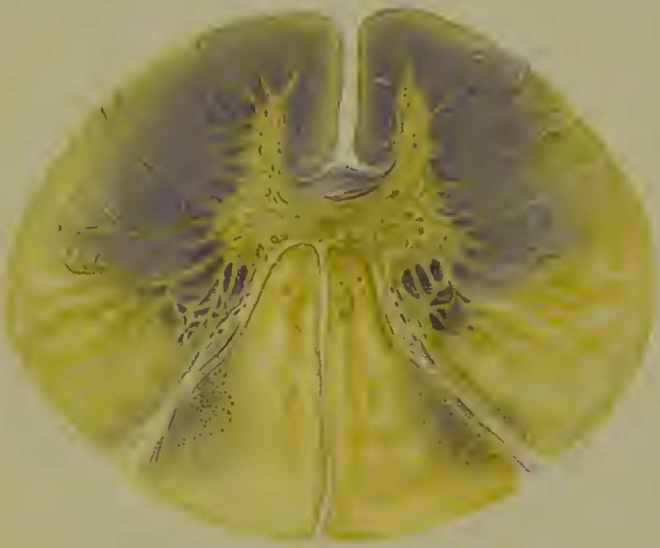

FIG. 302.—Combined posterior and lateral sclerosis (Collins).

Etiology.—The etiology of the disease is obscure. In many cases syphilis is the undoubted cause, but there are cases that cannot be referred to it. Other infections and perhaps intoxications may bring it about. The fact that hyaline changes in the blood vessels are so commonly associated with the disease might be interpreted to indicate that occlusion of the vessels plays an important part in the disease by shutting off the nutrient supply of the diseased areas.

Posterior Sclerosis or Tabes Dorsalis.—Degenerative and sclerotic changes of the posterior columns of the spinal cord are described as posterior sclerosis or tabes dorsalis. The clinical symptom-complex is known as *locomotor ataxia*.

There are three theories to explain to the origin of the disease: first, that it depends upon primary disease of the cerebral cortex; second, that it is a primary affection of the posterior columns; third, the newest and probably the best, that it depends upon primary disease of the posterior nerve-roots.

The cause of the disease is obscure. According to Erb, it is nearly always dependent upon syphilis. Traumatic lesions and infectious diseases are thought to cause it. The softening of the spinal cord that occurs in pernicious anemia affects by preference the posterior columns. Posterior sclerosis is also found at times in paresis. The lumbar seems to suffer more frequently and more severely than the dorsal, and the dorsal more frequently than the cervical cord.

There are no essentially peculiar features about the destructive changes. It is a chronic myelitis characterized by atrophy of the nervous substance and proliferation of the glia. The myelin sheaths first disappear, leaving the axis-cylinders denuded. Fat occurs in the tissue in molecular form, and is gathered up by leukocytes, which appear in considerable numbers in the lymphatics about the blood vessels. Amyloid bodies may be numerous. The nerve-fibers are slowly destroyed, many resisting destruction long after their myelin sheaths are gone. The neuroglia proliferation occurs in the degenerated and atrophic areas, and leads to the formation of coarser fibers than are usually seen, and later to contraction.

Starting at the lower part of the cord and ascending, we find that in the lumbar cord the degeneration affects the columns of Goll, the extreme anterior portions nearly always escaping; in the dorsal region there are, in addition, two areas of degeneration in the columns of Burdach; in the cervical region the chief seat of the disease is Goll's column and also Burdach's column, where some of the fibers are degenerated. In the neck one finds that, as a rule, two anterolateral areas of the column of Goll escape sclerosis.

The posterior nerve-roots are nearly always degenerated, and some believe this to be the starting-point of the disease. The ganglia on the posterior roots are frequently degenerated and their cells destroyed, and the degeneration has been traced for considerable distances into the peripheral nerves.

Degeneration of the sensory nerve-endings nearly always occurs.

It has also been found that the nervous lesions of tabes dorsalis are not peculiar to the spinal cord and peripheral nerves, but that the sclerotic process extends irregularly into the brain, where foci of gray degeneration or sclerosis may be found in the nervous substance and in the optic, oculomotor, and trigeminal nerves.

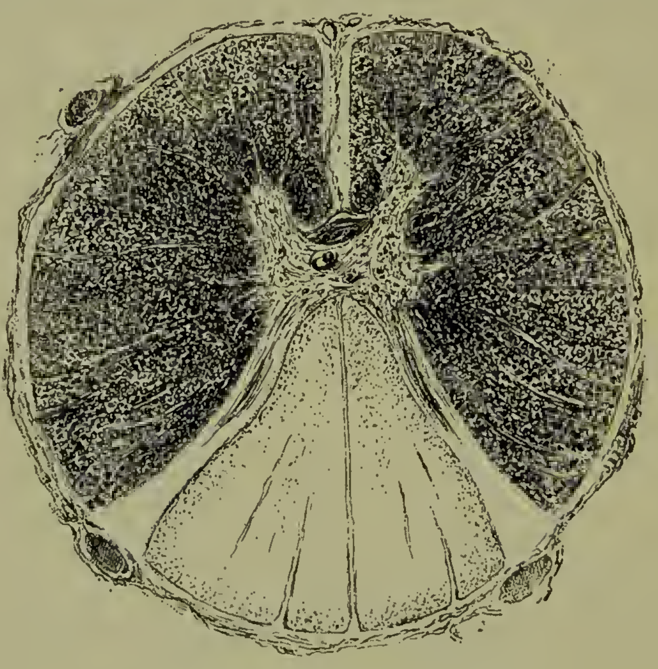

FIG. 303.—Tabes dorsalis (Collins).

The inception of the disease is gradual. No cases have yet been studied before the lesions were well defined. It is supposed to occur primarily in the spinal ganglia and posterior nerve-roots, and ascend these to the posterior horns of gray matter near Clarke's columns or to Burdach's columns. The affection of Goll's column may be a secondary ascending degeneration depending upon interruption of the fibers below. The cells of Clarke's column and the substance of the posterior horn of gray matter often suffer degeneration.

The disease is of indefinite duration, and is accompanied by a great variety of sensory disturbances, such as lancinating pains, girdle sensation, loss of patellar reflex, Argyll-Robertson pupil, diplopia, etc.

Friedreich's Ataxia.—Friedreich has described a hereditary form of posterior sclerosis now called by his name. The disease begins in childhood or early youth, and often affects several children in the same family. Except in minor details, the symptoms are similar to the locomotor ataxia of adults.

The disease is characterized by hyperplasia of the cerebellum or spinal cord, and by sclerosis of the posterior columns of the cord. The posterior sclerosis may, in rare cases, be absent. It usually affects the fibers of the column of Goll, and frequently also those of the column of Burdach. The cells of Clarke's vesicular column are likewise often degenerated. The fibers of the direct cerebellar tract also sometimes degenerate, and at times some fibers in the lateral pyramidal columns. Like the lesions of tabes dorsalis, the changes are most pronounced at the lower part of the cord, diminishing as the fibers ascend. The posterior roots of the spinal nerves are also degenerated, and some claim that there is degeneration of the sensory nerves.

The degeneration and sclerosis are of the usual type. If the nerve-fibers be not completely destroyed, they lose their myelin sheaths. Hyaline changes of the blood vessels are also frequent.

Acute Anterior Poliomyelitis.—This is a form of nervous degeneration and sclerosis the lesions of which are situated chiefly in the anterior horns of the gray matter of the spinal cord. It is principally a disease of childhood, though it sometimes affects adults.

Etiology.—The cause of the disease is unknown. It is almost universally recognized to be of infectious or toxic origin, and to result from the hematogenous distribution of its cause. It not infrequently results from exposure to cold, and sometimes occurs after attacks of the specific fevers. In many cases no cause can be assigned. The onset of the disease is usually rapid, and may be attended with general symptoms, such as chill, fever, etc. It may be a unilateral or a bilateral affection. It is rather more frequent in the lumbar cord than higher up, but may occur anywhere. It usually involves several superimposed segments of the cord, and may affect its entire length.

In cases in which the spinal cord can be examined a short time after the onset of the disease marked changes can be observed in the blood vessels, which appear much distended and surrounded by a zone of round-cells packed in the perivascular lymphatic vessels. The vessels chiefly affected are those of the anterior horns of the gray matter. Small interstitial hemorrhages are occasionally observed in the anterior horns. The tissue is usually observed to be softer than normal, and appears looser in texture and more or less infiltrated with small round-cells. Very interesting changes occur in the ganglionic cells, which are large, granular, clouded, often vacuolated, and irregular and peculiar in their staining reactions. The nucleus may be vacuolated and degenerated, and irregular distribution of chromatin occurs.

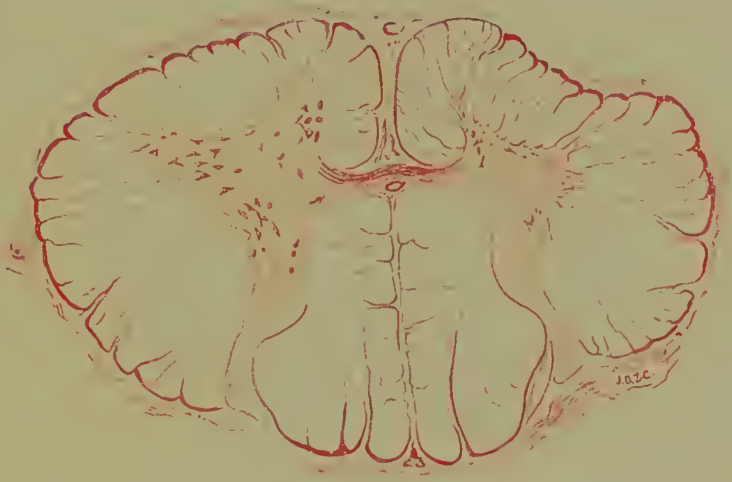

FIG. 304.—Chronic anterior poliomyelitis (Collins).

As the disease advances the cellular destruction becomes complete, and the ganglionic cells entirely disappear. The medullated nerves that enter and leave the gray matter lose their myelin sheaths and are altered in appearance. Some of the fibers are totally destroyed. Fatty molecules are liberated, and, appearing in the tissue, are gathered up by scavenger cells, so that fat-granule cells are rather numerous. Some or all the ganglion-cells may be destroyed according to the extent of the disease.

Later, the anterior horn of gray matter which has been the seat of the affection may undergo a gelatinous degeneration (colloid?), or a neurogliar hyperplasia may occur, by which the gray matter becomes indurated and actually sclerosed. Contraction usually follows this stage, and the gray matter of the affected part becomes shrunken.

The lesions, while they begin in the anterior horn of the gray matter, are not confined to it alone. It is true that in the posterior horn of the same side, and on the undisturbed side, there are a few if any changes, and the white matter of the cord escapes except for a few fibers of the pyramidal tracts which occasionally degenerate for a short distance. It is the anterior nerve-roots and motor nerves in which the secondary changes are observed. These consist of degenerations of some or many of the fibers, and are without special peculiarities.

The muscles to which the nerve-fibers distribute undergo a rapid atrophy, the change being in the nature of a fatty metamorphosis. If the patient lives and grows, the parts which were governed by the destroyed nerve-cells do not grow concomitantly, but have their development permanently arrested.

Chronic Anterior Poliomyelitis—Progressive Muscular Atrophy.—Chronic poliomyelitis differs from the acute form in that the disease is of insidious onset, chronic duration, occurs chiefly in adults, and is characterized by gradual atrophy and disappearance of the motor nerve-cells of the anterior cornua of the spinal cord. Sometimes the cells of Clarke's vesicular column are also affected. The nerve-cells gradually become smaller and smaller until they finally disappear. As the cells are destroyed a parallel degeneration or atrophy of the peripheral nerve, and of the muscles to which it is distributed, takes place. The atrophy usually affects first the muscles of the thumb and little finger, then the interossei, lumbricales, and other small muscles of the hand, spreading to the forearm and later ascending to the trunk. The atrophy may also begin in the lower extremities and ascend. It occurs by fatty metamorphosis of the muscular tissue.

Nowhere in the diseased tissues, either muscular or nervous, is there any sign of inflammation. The morbid changes are those of atrophy.

Etiology.—No cause is apparent, but analogy would indicate that some toxic or infectious condition was responsible for it. Sometimes the vessels of the anterior cornua show distinct changes. The disease usually begins in the cervical region of the cord, but may begin anywhere, and in the medulla is known as *bulbar palsy.*

Bulbar palsy, or **progressive glossolabiolaryngeal palsy,** is identical with chronic poliomyelitis anterior, except that instead of occurring in the cord it occurs in the medulla oblongata. Further, in place of the cells of the anterior horns of gray matter being affected, the disease is now centralized in the various nuclei of the medulla, which may be taken as their representatives, and affects the cells of the ganglia of the hypoglossus, glossopharyngeal, spinal accessory, vagus, facial, and other nerves.

The nerve-cells of the ganglia atrophy and disappear, the fibers of the various nerves degenerate secondarily, and a gradual atrophy of the voluntary muscles occurs in the distribution of the nerves.

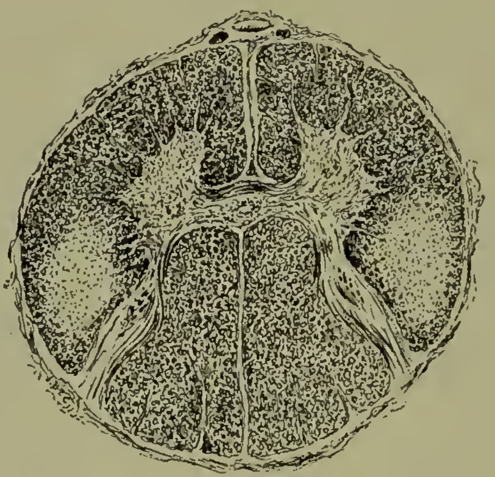

FIG. 305.—Primary lateral sclerosis (Collins).

Amyotrophic Lateral Sclerosis.—This is a spinal affection, which, in typical cases, adds to the atrophy of the ganglionic cells of the anterior cornua of gray matter, the degeneration of the peripheral nerves, and the atrophy of the muscles in their distribution, the additional lesion of a secondary (?) degeneration in the pyramidal tracts of the cord. The most variable part of the lesion-complex is the affection of the pyramidal tracts. It may be marked and extend high up the cord, pass through the medulla, and even continue to the internal capsule. In some recorded cases (Charcot, Marie) lesions of the cerebral cortex also occurred, as if the entire motor apparatus were involved.

According to Stengel, there is a case on record in which there was no lesion of the pyramidal tract. The degeneration of the pyramidal tracts affects fibers of both the anterior and lateral pyramidal columns. The degenerations are devoid of specific peculiarities.

The cause of the disease is not known. Syphilis is supposed to be of etiologic importance. Paralytic dementia may also be associated with it. In all probability the real injurious agent is some toxic substance generated within the body by its own processes or by infectious agents.

Secondary Degenerations of the Spinal Cord.—There are very constant degenerative changes observed to follow the path of certain systems of fibers, ascending or descending, when their connection with the ganglionic nerve-cells is broken. Such lesions may be of central or peripheral origin, and may be limited or extensive according to the individual case. The lesions may appear in a week, or sometimes less, after section of the cord. They may be visible microscopically in two days. The microscopic features of the degeneration have already been described. The nerve-fibers may completely disappear. The lesion occurs simultaneously in all parts of the affected nerve. After completion of the degenerative changes sclerosis with proliferation of the glia tissue occurs.

Descending Degeneration.—This form of degeneration very commonly results from disease of the cerebral cortex and internal capsule. It may succeed disease of any segment of the cord. The changes are observed in the pyramidal tracts, both anterior and lateral. If the lesion be unilateral and at a point higher up than the medulla oblongata, the anterior pyramidal tract of the same side and the lateral pyramidal tract of the opposite side will be affected. Inasmuch as a few fibers of the lateral tracts do not decussate, there may be degeneration in a few fibers of the lateral pyramidal tract of the same side also.

The degenerative changes extend downward to the end of the interrupted fibers in the anterior cornua of the gray matter, and occasionally these cells are found embraced in the resulting destructive process, undergoing atrophy and degeneration. The anterior nerve-roots and motor nerves have been known to show degenerative changes, so that a lesion of the cerebral cortex or internal capsule may be followed by degeneration of the entire remaining nervous communications.

When the lesion is in the spinal cord, the degeneration begins at the seat of disease and descends. Rarely, descending degeneration is also seen in the posterior columns. It usually affects a group of fibers that project backward and outward from the posterior gray commissure—the so-called "comma columns" of Schultze. These columns approach the posterior commissure more closely low down the cord, and form the oval fields of Flechsig.

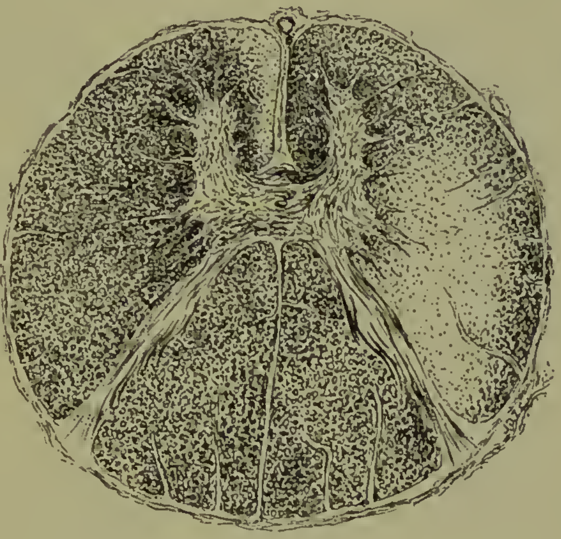

FIG. 306.—Descending degeneration after cerebral apoplexy (Collins).

Ascending Degeneration.—This usually succeeds transverse myelitis, and, ascending, affects the entire posterior columns in the lower part of the cord and the columns of Goll above.

Disease of the posterior nerve-roots, and especially of the spinal ganglia, is followed by ascending degeneration of the posterior columns. Sometimes ascending degeneration is observed in the direct cerebellar columns if the lesion producing it be in the upper dorsal region of the cord; in not infrequent cases it is associated with degenerations of the cells of Clarke's vesicular column. It may occur in the anterior lateral tract of Gowers.

The ascending degeneration usually terminates in the restiform bodies, but may continue on into the cerebrum (see Tabes Dorsalis).

DISEASES OF THE MEMBRANES OF THE BRAIN.

THE DURA MATER.

Hyperemia of the dura mater is not common, probably because of the hypostasis of blood in the vessels shortly after death, which causes the upper surface of the membrane to appear bloodless and the dependent part only to appear congested. The membrane is at best a comparatively bloodless, tendinous tissue.

Local hyperemias are sometimes observed about inflammatory foci, specific inflammatory nodes, or neoplasms.

Passive hyperemia sometimes results from the obstruction of the veins from thrombosis of the sinuses.

Thrombosis of the venous sinuses of the dura mater is a rather rare affection, seen in childhood after infantile diarrhea, in chlorosis and anemia, and in the terminal stages of phthisis, malignant diseases, and chronic wasting diseases. Such thrombi are known as marantic thrombi. Secondary thrombosis sometimes occurs as a result of the extension of inflammation from neighboring parts to the vessel-wall, as in internal ear affections, fracture of the skull, mastoid disease, etc. The thrombus is usually situated in the superior longitudinal sinuses, and may or may not cause death. Occasionally at autopsy coagula are removed from the superior longitudinal sinuses when least expected. These may have formed during the death agony. Their appearance differs from ordinary *postmortem* clots.

Hemorrhage from the vessels of the *dura mater* may be either internal or external, and usually results from traumatic injury. When associated with fracture of the skull, the hemorrhage from the dura mater is external, the blood flowing into the space between the dura mater and the bones. Much blood may escape, so that its pressure may compress the brain-substance. Such cases are described as *internal cephalhematoma*. Hemorrhages also occur in the dura mater itself, especially in persons who have died from suffocation.

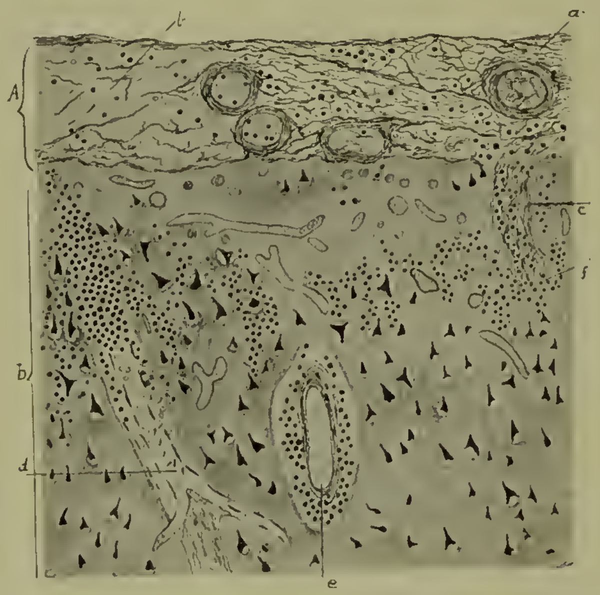

FIG. 307.—Acute meningitis and encephalitis: *A*, Pia mater; *a*, fibrinous exudate; *b*, hemorrhagic exudate; *B*, cortical substance of the brain; *c*, small blood-vessel filled with fibrin and infiltrated with leukocytes; *d*, longitudinal section of a small vessel whose lumen and perivascular space are filled with leukocytes and red blood corpuscles; *e*, blood-vessel with many leukocytes in the perivascular space; *f*, collection of leukocytes in the cerebral substance (Weichselbaum).

Acute pachymeningitis, or acute inflammation of the dura mater, usually follows traumatic injuries of the skull with infection. It may also succeed middle-ear disease and other suppurations of contiguous tissues. It is characterized by suppuration. The membrane is creamy white, unless the occurrence of hemorrhage discolors it, and is covered with a layer of pus.

Chronic internal pachymeningitis is a not infrequent affection, not perfectly understood, but apparently of hematogenous origin. It is accompanied in most cases by more or less disease of the arachnoid and pia.

The lesion consists of the formation, one after another, of delicate lamina of fibrinous exudate upon the inner surface of the dura mater. These, when examined microscopically, are found to be composed of fibrin threads and granules with a few leukocytes. In the course of time the fibrin disintegrates and is absorbed, but simultaneously there are proliferation of the connective-tissue cells, fibroblastic processes, and the gradual formation of a delicate connective tissue which replaces the original fibrin. Newly formed capillaries vascularize the tissue, sometimes to an abnormal degree.

Not infrequently the capillaries seem to be abnormal in development or subject to subsequent disease by which extravasations of blood occur into the interstices and between the lamina of the tissue, causing it to become of a deep rust-red color and hemorrhagic appearance to the naked eye, and full of amorphous blood-pigment when examined microscopically. Cases of this kind are frequent among the insane, in alcoholics, and in cases of chronic cardiac and renal disease. The frequent escape of blood gives the disease its familiar name, *hemorrhagic pachymeningitis.*

In the development of the connective-tissue lamina the capillaries are sometimes destroyed, so that the tissue becomes avascular. This, however, does not terminate the process, for, as it happens in one area, further proliferation of capillaries and hemorrhage occur at others. Considerable-sized hemorrhages, in the dura, in this affection, are called *hematomata* of the dura mater. The absorption of the hemorrhagic exudate takes place slowly. Calcareous infiltration is sometimes seen in the diseased tissue. The hemorrhagic pachymeningitis usually corresponds to the distribution of the middle meningeal artery. It is bilateral in about one-half of the cases.

Chronic pachymeningitis externa, in which the inflammatory changes are observed on the outer surface of the dura mater, is less frequent. It may not only bring about changes in the dura mater itself, but may also occasion absorptive changes in the bones of the skull.

Calcification of the dura mater is very frequent and varied. In the aged the external surface of the dura is sometimes found covered with calcareous plates similar to fish-scales.

Diffuse calcareous infiltration in the form of amorphous granules also occurs in chronic pachymeningitis.

Probably the most frequent, though least important, form of calcification occurring in the dura is the formation of *osteophytes*—bony tumors—in the falx cerebri. These may be irregular, shapeless, somewhat flattened masses of irregularly formed bone in the dura mater, or may correspond to the sickel-shaped outline of the falx.

Tuberculosis of the dura mater is not very common. It may succeed tuberculous disease of the bones of the skull, may extend to the dura from tuberculous disease of the brain, pia, and arachnoid, or may be of hematogenic, metastatic origin. The tubercles form chiefly upon the inner surface of the membrane, and present the usual appearance of miliary tubercles. Large tuberculous growths form characteristic cheesy masses, but may at times somewhat resemble sarcoma.

Syphilis of the dura mater may lead to diffuse cellular infiltration, adhesions between the dura, arachnoid, and pia, and may be the cause of diffuse fibrous thickenings of the membrane—*pachymeningitis fibrosa.* Sometimes the fibrous masses contain cheesy masses—old gummata (?).

Gumma of the dura is rare. The lesions are of various size, usually flattened, and caseous and apt to be surrounded by rinds of dense connective tissue.

Tumors of the Dura Mater.—The most frequent tumor is *spindle-cell sarcoma. Round-cell sarcoma* is also seen. The *alveolar sarcoma* is not rare. The tumors usually form more or less well-circumscribed nodes or flattened growths, which project upon the inner surface of the membrane and press upon the brain. They vary from the size of a pea to that of an orange. Occasionally they develop upon the outer surface of the dura, and by pressing upon the bones, lead to absorption and ultimate perforation. The *endothelioma* is frequently observed upon the inner surface of the dura mater. It has its usual characteristics (*q. v.*). Sometimes the sarcomata of the dura are telangiectatic, sometimes they assume the form known as *angiosarcoma*. The hyaline degeneration of the blood-vessel walls which characterizes *cylindroma* is also frequently seen. *Psammoma* is of not infrequent occurrence, both in the simple form and in combination with sarcoma (*psammosarcoma*). *Fibroma* and *lipoma* are rare.

Secondary growths of the dura mater may occur. Of these, sarcoma and gliosarcoma from the brain may be mentioned, and also secondary carcinoma and epithelioma from various neighboring regions.

Parasites of the dura mater are very rare. Birch-Hirschfeld mentions the echinococcus and Cysticercus cellulosa as having been observed.

THE PIA MATER AND ARACHNOID.

Anemia of the pia mater is very rare. General anemia and fatal hemorrhage are supposed to cause it. In reality in fatal hemorrhage with profound anemia of other organs the meninges are not infrequently somewhat congested.

Hyperemia.—Active hyperemia of the pia is frequent, forming the earliest stage of meningitis. Active hyperemia also occurs in death from alcoholism and during epileptic attacks. It also is frequent in typhoid, hydrophobia, cholera, and other infectious diseases, and in such intoxications as lead, morphin, etc. Acute congestion of the meninges is sometimes seen in acute mania.

The macroscopic appearances are not difficult of recognition. The entire pia mater will show a rosy-red color, depending upon general turgescence of the vessels. All the visible vessels are injected, and it is very evident that arterial hyperemia is present. It is not always easy to differentiate between an acute congestion and an early inflammation, and it may require a microscopic examination to determine it. The cerebrospinal fluid may appear slightly clouded in acute congestion.

Passive hyperemia, or venous congestion, is recognized with somewhat greater difficulty because of the frequency with which the vessels of the pia are found engorged with blood after death. It is true that the *postmortem* congestion is chiefly in the dependent part of the vascular network, but still it is sometimes difficult to decide whether a certain amount of venous congestion found at autopsy is normal or not.

The venous congestion is most easily observed in the larger veins, which are full and tortuous. In cases of chronic venous congestion, such as follows heart disease, emphysema, etc., these veins become quite ectatic and unusually tortuous. The arachnoid is nearly always clouded in passive hyperemia, and the amount of fluid is increased.

The causes of chronic congestion of the pia mater are heart disease with hypertrophy and increased arterial pressure or venous obstruction. The obstruction to the escape of the venous blood from the cavity of the skull because of diseased bones, diseased or thrombosed vessels, congestion of the larger veins, pressure of tumors, etc., all predispose to passive congestion of the pia and brain substance.

Edema of the meninges is seen as an increase in the cerebrospinal fluid that occupies the subarachnoid space. It occurs in all cases of hyperemia, both active and passive, and in all forms of acute inflammation. It is sometimes spoken of as *hydrops meningeus*. Meningeal edema is sometimes seen in nephritis, probably being of toxic origin. Large collections of fluid in the spaces between the pia and arachnoid are described as *hydrocephalus externus.*

Hydrops ex vacuo is a form of edema or dropsy of the arachnoid which is seen in consequence of atrophy or hypoplasia of the cerebral convolutions. The space that should be occupied by the normal brain tissue is found filled with fluid. In all forms of meningeal edema the arachnoid is swollen and gelatinous in appearance.

A **gelatinous edema** of the pia and arachnoid, with slight clouding of the membranes, is found in *paresis* and some forms of *insanity*.

Hemorrhage.—Subarachnoid hemorrhages from the vessels of the pia mater are of various origin and extent. Small punctiform hemorrhages are not infrequent as a result of inflammation, and are at times so numerous as to warrant the description *hemorrhagic meningitis.* Anthrax infection of the pia and arachnoid frequently causes the hemorrhagic form of the disease. Scurvy, hemophilia, various infections, and some toxic conditions may also lead to local blood extravasations.

Hemorrhagic collections between the pia and arachnoid are usually more massive and conform in shape to the sulci of the cerebrum, because of the peculiar arrangement of the arachnoid, which is firmly united with the pia where it is in contact with it upon the convolutions, but separated from it where the pia dips down into the sulci. It is in these open intervals that the hemorrhage occurs. The hemorrhages follow severe injuries of the skull with or without fracture.

Massive hemorrhages into the subarachnoid space usually result from the rupture of aneurysms of the larger cerebral arteries and the entrance of the blood into the space between the pia and arachnoid, covering the greater part of the brain with a thin layer of blood. Such hemorrhages do not need to be superficial, but may occur in the brain substance or in the ventricles, from which the blood flows along the choroid plexuses until it finally works its way into the subarachnoid space. The fluidity or solidity of the blood in such cases is an index of the duration of the case.

Leptomeningitis, or inflammation of the pia mater and arachnoid, may be either acute or chronic.

Acute leptomeningitis is probably always an infectious inflammatory affection resulting from the presence of micro-organisms brought to the tissues by the blood, by accidentally or surgically inflicted wounds, by extension to the meninges along the lymphatics, or by continuity of tissue from the ear, the orbit, the nasal fossæ, the frontal sinuses, etc.

Various micro-organisms may cause the affection, but the *pneumococcus* is that most frequently found. The streptococci and staphylococci of suppuration, the typhoid bacillus, influenza bacillus, the Bacillus pyocyaneus, the Bacillus coli communis, the bacillus of Friedländer, the bacillus of bubonic plague, the glanders bacillus, tubercle bacillus, and the actinomyces have all been observed. Among the epidemic cases it is usual to find the meningococcus (Diplococcus intracellularis meningitidis) of Weichselbaum, which is now recognized to be its cause.

The **Diplococcus intracellularis meningitidis** of Weichselbaum, the now accepted cause of cerebrospinal meningitis, especially the epidemic form, is supposed to enter the membranes of the brain from the nasal fossæ or other opening of the skull.

Morphology.—The organism is a diplococcus having somewhat the biscuit shape of the gonococcus, a resemblance which is increased by the fact that the cocci commonly occur inclosed in the cytoplasm of leukocytes. Weichselbaum, who first observed the arrangement, found it constant in sections of the brain and its membranes, though in the exudate of the disease a large number of free cocci also occur. It was because of the presence of the cocci in the leukocytes that he decided to call it *intracellularis.*

The organism is non-motile and without spores or flagella.

Staining.—It readily stains with the ordinary dyes, and probably not by Gram's method.

Cultivation.—The organism is of feeble vegetative power, and does not adapt itself easily to artificial conditions of cultivation. It grows upon agar-agar, glycerin agar-agar, Löffler's blood-serum mixture, and a few other media. It does not grow in bouillon or on potato or gelatin.

The cultures have no characteristic appearance; the cocci grow sparingly and only at body-temperature, forming a more or less confluent series of minute, rounded, grayish points, easily overlooked upon opaque media like blood-serum. The general characteristics of the growth are like those of the pneumococcus and streptococcus.

Upon plates the colonies are irregularly rounded and granular. Those at the surface are largest, and contain a yellowish-brown central nucleus. The edges may be dentate. The colonies are grayish or yellowish at the center, becoming less intense toward the edges.

The vitality of the organism seems low, so that it soon dies out in artificial culture-media, and when under study, requires transplantation every day or two. The organisms are usually sparingly, but sometimes plentifully, found in the fluid secured from the spinal canal by lumbar puncture.

Pathogenesis.—The presence of the coccus in the exudate of cerebrospinal meningitis is so constant that its etiologic rôle cannot be doubted. It does not, however, produce characteristic lesions in animals. Weichselbaum trephined animals and introduced the cocci beneath the dura, some of them dying from the resulting congestion and suppuration of the membranes.

Distribution.—The organism is known to us only as a parasite of man. It was isolated by Scherer from the nose in coryza, from the conjunctiva by Fränkel and Axenfeld, and from cases of ostitis and rhinitis by Jäger, but with these exceptions it is known only in cerebrospinal meningitis. It occurs in over one-half of the examined cases of cerebrospinal meningitis.

The infections are very often pure, though it is not unusual to find the streptococci and staphylococci together with others upon the list.

In studying the lesions of leptomeningitis it is convenient to divide them into groups according to the character of the exudate formed. It is also customary to separate the simple and infectious (epidemic) forms. As, however, the lesions of the ordinary and epidemic forms are almost identical, they will not be separately considered here. It is quite probable that the following familiar groups are simply different stages of the same process and the divisions are made solely for convenience of description.

Serous Leptomeningitis.—This is a rapidly fatal form of the disease in which death occurs before suppuration has had time to develop. It is rather more frequent in children than in adults, and not infrequently occurs in the early days of infectious diseases, such as measles and scarlatina. In the adult it is occasionally seen after sunstroke.

The morbid anatomy is simple, and consists in an edematous infiltration of the pia and arachnoid, accompanied by marked hyperemia and the collection of a serous fluid in the subarachnoidal space and ventricles of the brain. The fluid may appear slightly clouded, and is rarely present in considerable quantity.

Microscopic examination shows the presence of large numbers of leukocytes in the fluid and in the perivascular lymphatics.

Fibrinopurulent Leptomeningitis.—This is probably a more advanced stage of the serous form, and differs from it in the occurrence of suppuration and in the presence of fibrin.

The appearance of the brain is, however, quite different and very characteristic. Its essential feature consists in a collection of purulent material in the subarachnoidal space. It is chiefly observed and first noticed in the depressions of the sulci and along the lines of the chief vessels. As the pus increases in amount it fills the subarachnoidal space so as to form yellowish bands between the convolutions, and finally, when present in extreme amounts, to coat the entire surface of the hemispheres with a yellowish, creamy layer, in which much or little fibrin may form and make the mass coherent.

The inflammatory process may be local or limited when it spreads from a local area of bone-disease, or may be common to both hemispheres. It may occur at the vertex (*cortical meningitis*) or at the base of the brain (*basilar meningitis*). When there is much pus, it often finds its way through the transverse fissure into the ventricular cavities, and appears as an infiltration following the course of the choroid plexuses. Ependymal inflammation nearly always occurs, and the fluid of the ventricles becomes turbid.

When the inflammation is very active, it is not rare to find small hemorrhages, causing discoloration of part of the exudation. In extreme cases the exudate may be so thick as entirely to obscure the convolutions, making the brain appear like a smooth yellow or buttered mass. The pus occupies the delicate tissue of the pia and arachnoid, the subarachnoidal space, and the loose tissue surrounding the blood vessels. In marked cases it may begin to invade the central cortex, in which degenerative changes, such as destruction of the axis-cylinders, degeneration of the ganglion-cells, etc., become apparent. It is not infrequent to find the chief distribution of the disease along the middle meningeal artery.

The exudate is yellowish and creamy in cases depending upon the streptococci and staphylococci; contains more fibrin in cases caused by the pneumococcus. Cases associated with the Bacillus coli communis are frequently foul-smelling.

It is not always possible to determine the etiology of the case from the characteristics of the exudate present. Green pus, for example, is quite frequent irrespective of Bacillus pyocyaneus. In cases of actinomycosis the actinomyces grains may be present.

Epidemic cerebrospinal meningitis seems to begin at the frontal lobes and gradually extend backward and downward, affecting the inner membranes of both brain and spinal cord. It is very frequently of a type spoken of as *fulminant* or *foudroyant*, and is likely to bring about death before much suppuration has occurred. The exudation is chiefly basilar and spinal, the base of the brain and the posterior surface of the spinal pia being coated with a yellowish layer, giving it a "buttered" appearance. It is in these cases that Diplococcus intracellularis meningitidis is found.

Purulent leptomeningitis is commonly fatal. It may, however, recover by absorption of the exudate and gradual return to the normal condition. It is not uncommon to find certain permanent alterations following the disease. Of these, the union of the pia and arachnoid, fibrous adhesions between pia, arachnoid, and dura mater, and general fibrous thickening of the pia and arachnoid may be mentioned. In cases in which the disturbance within the ventricles has been considerable, permanent dilatation of the ventricles may remain.

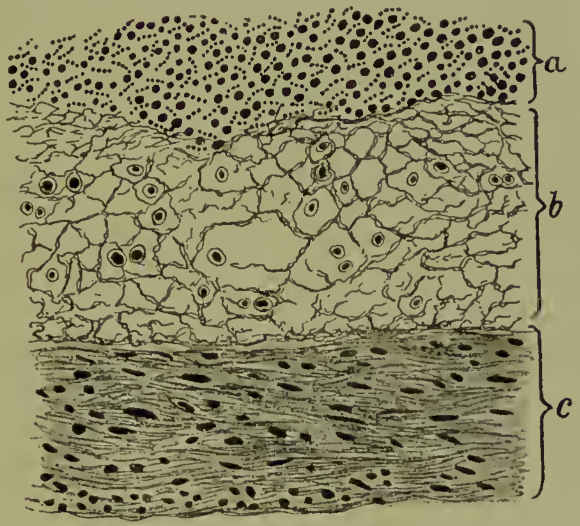

FIG. 308.—Fibrinopurulent leptomeningitis: *a*, Purulent exudate rich in streptococci; *b*, fibrinous exudate; *c*, dura mater with some leukocytic invasion (Weichselbaum).

Chronic leptomeningitis is a rather indefinite term, used to describe a variety of different conditions. By some it is thought that the Pacchionian granulations or enlarged papillæ of the arachnoid, which appear upon the dura near the great longitudinal sinus, result from chronic inflammation, but they are so common that it is no doubt incorrect to look upon them as abnormal. Some look upon indurations of the pia mater resulting from previous acute leptomeningitis as indications of chronic leptomeningitis, when, in fact, they may simply depend upon cicatricial formations occurring during convalescence. Still others, more correctly, restrict the term to the progressive changes occurring about chronic specific inflammations, such as tuberculosis, and about neoplasms. Here we have a true chronic inflammatory process, characterized by round-cell infiltration, connective-tissue hyperplasia, and induration.

In *paretic dementia* chronic disease also takes place in the pia mater and arachnoid. It consists of thickening of the membranes seemingly beginning in the frontal lobes, and extending backward. The pia is distinctly clouded, and may be white and opaque, chiefly in the sulci, but also upon the convolutions. The disease spreads to the central lobes and opercula, and sometimes farther back. The tissues affected are infiltrated with round-cells and undergo connective-tissue proliferation. There are occasional collections of erythrocytes, which probably escape from the blood vessels by diapedesis, and, by disintegration, cause a brownish or yellowish pigmentation, particularly observable in the adventitia of the blood vessels descending into the brain substance below. The disease seems to descend from the pia to the subjacent cortex, and even to the white matter of the brain, especially along the blood vessels, leading to what is described as *meningo-encephalitis*. The process is never evenly or regularly distributed, but occurs in the form of scattered collections of cells about a limited number of blood vessels. Some of the affected vessels become hyaline, others become thickened.

Tuberculosis of the Pia and Arachnoid.—Tuberculous meningitis occurs both in children and in adults, but most frequently in the former. It may affect all parts of the meninges, but seems to have a preference for the basilar portion. It may succeed primary tuberculosis of the dura or of the brain, but more frequently is of secondary hematogenous origin, following tuberculosis of the lungs, etc. In rare cases it seems to be a primary affection.

The lesions are typical miliary tubercles occurring chiefly at the base of the brain, especially upon the pia mater covering the pons, about the optic chiasm, the Sylvian fossæ, and the perforated spaces.

In tuberculous meningitis of hematogenous origin the lesions are situated in the pia mater and in the subjacent cerebral tissues. They are best seen upon the inner surface of the membrane, and cluster about the walls of the blood vessels, consisting at first of cellular infiltrations and thickenings of the walls of the vessels.

The disease is of rapid course, and usually terminates fatally. Many cases are characterized by a serous or seropurulent exudation beneath the arachnoid, as well as by tubercle formation in the membranes. Sometimes there is mixed infection, due to the presence of the pneumococcus. Uncomplicated tuberculosis, however, may show the exudate. This exudation may be quite marked. The disease may also extend along the pia into the transverse fissure, and affect the choroid plexuses in the ventricles and the ependyma.

Tuberculous meningo-encephalitis is not infrequent. The arteries of the anterior and posterior perforated spaces often show little gray tubercles when carefully withdrawn from the tissue, even though no tubercles can be found elsewhere. The disseminated miliary tubercles are nearly always small, the patient dying before they have time to become large.

In primary tuberculosis of the meninges a single lesion may attain considerable size without causing serious symptoms. Such *solitary tubercles* may attain the size of a hen's egg, and are called *tyromata*. They are situated in a depressed, atrophic area of the brain, though by uniting with it the tubercles may extend into the cerebral substance. Such large masses are grayish or yellowish white, cheesy, and usually firm, though sometimes soft and semifluid.

In rare cases such large tuberculous masses undergo calcareous infiltration. Though the center becomes calcified, about it there is a zone of extension with pinkish granulation tissue, in which a number of typical, fresh tubercles are present. The large masses readily sink into and replace the soft brain substance, and so do not come into contact with the dura. If, however, they touch it, union and subsequent invasion of the dura take place.

Large tuberculous masses may persist for a long time without metastatic distribution through the lymphatics, either to the brain or meningeal tissues. On the other hand, such extension may occur early.

Tuberculous lesions of the pia depending upon diseased bones, etc., occur first near the point of infection, and may either spread slowly, forming considerable-sized local lesions, or rapidly, with disseminated tubercles.

Syphilis of the meninges is chiefly characterized by gumma formation. Cellular infiltrations may, however, occur and form a conspicuous part of the process. A perivascular round-cell infiltration gradually develops into a diffuse cellular infiltration, with subsidiary perivascular collections. Increase in size of the chief cellular collection leads to the final formation of a partially vascularized node. Caseation or gummy degeneration of the node, succeeded by cicatrization of its borders, ultimately produces a dense cicatricial formation. Thickenings of the intima of the larger blood vessels may be observed. The lesion may be small or large. Characteristic gummata may form. In the latter case it extends from the pia and invades the cerebral substance. The lesion is not easily recognized, except when typical gummata are present. It may assume the form of distributed thickenings of the pia, with cicatricial formations in the sulci upon the surface of the brain, and sometimes takes the form of wide-spread chronic leptomeningitis.

Tumors of the Pia and Arachnoid.—*Pacchionian Bodies.*—Pacchionian bodies grow from the arachnoid in the form of small, rounded, circumscribed, more or less pedunculated, dense fibrous projections, usually quite numerous and chiefly observed above the great longitudinal fissure of the brain. By growing into the dura mater they bring about a firm union of the two membranes. Not infrequently they slowly work their way through the tissues of the denser membrane into the longitudinal sinus and upon the outer surface of the membrane. In the sinus they cause no disturbance of the circulation. Upon the external surface of the brain they are very prone to unite, making a rough grayish or whitish mass extending along the angle formed by the convex and median surfaces of the brain at the vertex of the skull. Here dura and pia are very intimately adherent. When large and collected into little masses projecting externally, their contact with the bones of the skull is followed by atrophy, so that the osseous tissue may be honey-combed along the line of the sagittal suture, or may present occasional deep excavations the surfaces of which are reduced to a thinness little more than that of paper.

Pacchionian granulations are without pathologic or clinical importance. They are observed in nearly every adult body examined after death.

Endothelioma is of frequent occurrence in the soft membranes of the brain, where it develops from the cells of the lymphatics (*lymphangiosarcoma*) and sometimes from the perithelial cells. The tumors may be small, but not infrequently attain the size of a hen's egg. They are not usually circumscribed, but frequently extend irregularly in all directions by more or less well-developed prolongations. Their development occurs chiefly from the pia and arachnoid. Microscopically they are characterized by spaces lined with cells somewhat similar to those of tubular glands. Few of the spaces show such a regular arrangement, however, and most of them are filled with irregularly proliferated cells.

Simple connective-tissue tumors are occasionally seen in the pia and arachnoid. Among them are *fibroma*, *myxoma*, *lipoma*, and *osteoma*. Organized thrombi may sometimes be mistaken for fibroma. *Lipoma* is very rare in all parts of the nervous system.

Sarcoma of the pia and arachnoid is said in its early stages to resemble endothelioma or perithelioma, and may develop from the same elements. *Angiosarcoma*, *myxangiosarcoma*, and *cylindroma* are also rather frequent growths.

Psammoma and **psammosarcoma** are rather less frequent in the pia and arachnoid than in the dura mater.

Epithelioma.—True epithelioma of the pia mater is rarely seen. It usually occurs in the interior of the brain, and seems to grow from the epithelium covering the choroid plexuses or from the ependyma. The tumors are soft. They may attain considerable size, and show malignancy, both by the disintegration of the tissue in which they grow and by metastatic growths in remote parts of the brain. The tumor has its usual characteristics, and consists of a delicate stroma of connective tissue with very numerous epithelial cell masses inclosed in irregular spaces. The cells are, for the most part, of the columnar type, though one not infrequently observes laminated masses of flattened cells analogous to the epithelial pearls of squamous epithelioma. The tumor not infrequently occurs in a papillary form, and projects into the ventricle in a dendritic form. It is prone to retrogressive changes, of which the most frequent is myxomatous degeneration of the stroma.

Cholesteatoma is an infrequent tumor of the pia mater. It is more frequent at the base of the brain than elsewhere, and is seen chiefly upon the pons, in the Sylvian fossa, and in the cerebellum, though it sometimes occurs in the ventricles. It may attain the size of an apple, but is far more frequently the size of a pea. It is sometimes smooth, sometimes nodular, and the surface may be shining.

Teratomata, tumors composed of all the body tissues heterogeneously massed together, are rarely seen. They occur in the meninges, in the ventricles, and sometimes in the hypophysis cerebri. The origin is unknown. Clinical evidences of their presence is usually early manifested.

Secondary tumors of the membranes of the brain are by no means infrequent, and result from metastasis. *Sarcoma, carcinoma,* etc., occur. They may take on a wide-spread development in the subarachnoidean space.

Cysts sometimes occur in the choroid plexuses, as *exudation cysts* (the choroid plexuses are supposed to secrete the cerebrospinal fluid). *Parasitic cysts* resulting from the Cysticercus cellulosæ have also been observed. A *dermoid cyst* of the choroid plexus has also been observed.

Parasites of the meninges are rare. The only forms that need be mentioned are the echinococcus and the Cysticercus cellulosæ.

THE BRAIN.

Congenital malformations of the brain may involve the cerebrum or cerebellum. This may or may not be accompanied by changes in the bones of the skull.

Deformities of the Skull and Brain.—Of these, may be mentioned absence of the cranium—*acrania;* ununited sutures—*cranioschisis;* cleft skull and spine—*craniorrachischisis;* and local irregularities of ossification. The results will vary according to the exact condition present, so that the brain may be completely or partially undeveloped—*anencephalia;* or may project through fissures or openings, forming hernia—*cephalocele.*

In *acrania,* although the bones of the skull are absent, the brain is represented by occasional small collections of nervous tissue, or a small mass at the basilar process of the occipital bone; in *acephaly,* the membranes are present and form a sac filled with clear fluid. At times the membranes seem to have ruptured and collapsed. When the cerebrum and cerebellum are entirely absent, the pons and medulla are often present. When the cranium fails to develop on one side—*hemicrania*—the brain of that side is undeveloped. It is not usual for the remaining side of the brain to be well developed under these conditions, so that at least a partial anencephalia is almost invariable.

Deformities of the Brain Depending upon Malformation of the Cranium.—*Cranioschisis* is most frequent between the frontal bones and in the neighborhood of the posterior fontanel in the posterior part of the occipital bone. It may occur in the sagittal suture or in the sphenoid bone. If the meninges project through the fissure, the condition is spoken of as *meningocele.* If the brain substance also escapes, *encephalocele* or *encephalomeningocele.*

It is not impossible that the clefts in the bones may result from dilatation of the ventricular cavities of the brain and separation of the bones during fetal hydrocephalus. Large meningoceles and encephaloceles are not subject to surgical interference and are usually incompatible with life. Small lesions of this nature are not infrequently cured by the surgeon.

The hernias are described as frontal, occipital, anterior, posterior, superior, lateral, etc. Fissures of the sphenoid are usually accompanied by cleft-palate and harelip. Sometimes the anterior cerebral vesicle does not develop properly, and fusion of the frontal lobes takes place. There may then be a single, imperfectly formed eye. This condition is described as *cyclencephalia.*

Hypoplasia of the brain must necessarily follow early union of the cranial sutures, but whether or not hypoplasia always depends upon this cause, must be regarded as an open question. Virchow was of this opinion, but Cruveilhier and others incline toward the view that micro-encephalia depends upon previous intra-uterine *hydrocephalus externus,* by which the development of the surface of the brain is retarded by pressure.

The brain in microcephalia is smaller than normal, but the parts are properly proportioned. The convolutions are usually less numerous and less complex than in the normal brain. The convolutions may be as complex as normal, but are abnormally narrow. This condition is called *microgyria.* In rare cases the convolutions become membranous in character, and are so attenuated as to contain scarcely any nervous substance. The microgyria is not only a gross morbid lesion, but is one that affects the finer structure of the brain as well, being characterized by loss of some of the cortical layers, diminution or total absence of nerve-cells, etc. The brain may weigh from 200 to 900 grams less than the normal brain.

The hypoplasia is not always symmetric, but sometimes affects lobes of the brain singly and unilaterally. The convolutions of the affected area are usually very narrow. The condition may affect either cerebrum or cerebellum. Its remote effect is sometimes seen in the spinal cord. Thus, if the motor area be not developed, the pyramidal tracts are often absent. Absence of columns of the cord is likely to result in micromyelia.

A true aplasia of the nervous tissue sometimes leaves the brain with distinct holes or depressions in its substance. These may communicate with the lateral ventricles, or may be separated by a very thin layer of white matter. Neighboring convolutions are not particularly disturbed. The condition is known as *porencephaly*. Some writers look upon it as the result of cerebral softening following anemic infarcts. The absent tissue is sometimes partly replaced by fibrous or cystic outgrowths from the pia mater.

Congenital absence of parts of the brain other than the convolutions may also occur. Of these may be mentioned *absence of the corpus callosum*. It may take place in brains otherwise deformed or in brains otherwise normal. It is invariably associated with absence of the callosomarginal sulcus, vertical division of the fornix, and more or less secondary degeneration.

Absence of one or both hemispheres of the cerebellum is sometimes observed. It is said to be accompanied by sclerotic changes, though collections of cerebrospinal fluid usually replace the lost tissue. With the absence of cerebellar tissue very small olivary bodies, reduction in the size of the pons and medulla, and occasional abnormalities in the corpora quadrigemina may be observed.

Sometimes the convolutions are anomalous. When these pertain to minor convolutions only, no attention need be paid to them. Rarely they affect the major landmarks of the brain. Thus the fissure of Rolando is sometimes interrupted by gyri,—*annectant gyri*,—or the parieto-occipital fissure, which is normally interrupted, may be free. In all probability these changes are of no clinical or pathologic significance.

Hydrocephalus.—Hydrocephalus, or *water on the brain*, is a collection of fluid in the ventricles of the brain or in the subarachnoid space. It may be *external*—that is, outside of the brain in the subarachnoidean space; or *internal*, and distend the ventricular space. It may be *congenital* or *acquired*.

External Hydrocephalus or Meningeal Hydrops.—Sometimes this forms what is described as *hydrocephalus ex vacuo*, and is simply an exudation of fluid to replace or fill up gaps left in the cerebral substance where tissue is absent.. It is not always possible to tell whether external collections of fluid are primary or whether they are of secondary origin, and it may be that in the cases spoken of as hydrocephalic micro-encephalia the primary hydrocephalus is the cause of the hypoplasia of the brain. Such a condition may also be the cause of anencephalia.

Internal hydrocephalus is a fluid collection within the ventricular cavities (third and lateral ventricles) of the brain. All degrees may occur. It may at times seem to be limited to a ventricle, or it may fill all the ventricles with a fluid collection under considerable pressure; it may moderately dilate the ventricular cavities, or it may so greatly distend the general ventricular space as to transform the hemispheres of the brain into a thin-walled sac. Of the communicating ventricles, the fourth is always least affected. The fifth ventricle takes no part in the process. It usually begins in intra-uterine life, sometimes quite early, but may also develop after birth. It may run its whole course before the completion of gestation, and produce an enormous head that interferes with delivery; or may, after a somewhat different course, result in anencephalia.

As a rule, the disease is bilateral and symmetric. If the child be safely born, the subsequent course of the case may result in a head enormous in size from distention of the cranium by the pressure of the fluid accumulation within the ventricles. The bones of the skull in these cases are widely separated at the sutures, the spaces being filled by Wormian bones. The dura and pia mater are distended into great sacs, and from the thinned cerebral tissue the feebly developed convolutions are pressed flat. The cortical substance of the brain may measure only a few millimeters in thickness.

The fluid occupies the lateral and third ventricles and may dilate the aqueduct of Sylvius. It rarely dilates the fourth ventricle, however. The fifth ventricle may dilate or its walls may atrophy and permit free communication of the lateral ventricles. It may dilate the infundibulum and form a small sac at the base of the brain. The fluid is clear and watery. The choroid plexuses are usually enlarged and pale and may be cystic.

The appearance of the child with hydrocephalus is quite characteristic. The head is large and globular, the face small, the forehead high and bulging, and the eyes may project and the sutures gape. When the brain is removed and examined, it is usually found to have about the normal relative weight. It is pale and anemic, and feels soft and flabby. The interior is smooth, or may show nodules from sclerotic areas beneath the ependyma. The choroid plexuses of the ventricles are somewhat hypertrophied, and appear pale and are often cystic. The corpus callosum is apt to become very thin. When, from any cause, the surface of the brain is compromised and its tissues lost, secondary degeneration may be noticed in the cord. Chiari has also observed slight changes in the cerebellum in hydrocephalus.

The cause of hydrocephalus is not known. Stengel regards it as of parental origin, and points out that the children of drunkards are apt to suffer from the affection. It is commonly regarded as of inflammatory origin. It may have some connection with closure of the transverse fissure of the brain, which prevents the exit of fluid from the ventricles. Some writers find the cause of hydrocephalus in an alteration in the blood pressure of the choroid plexuses and in the cerebral veins.

Marked hydrocephalus is usually fatal, yet in most almshouses and asylums one or more hydrocephalic adults are found, attracting attention because of the enormous size of their heads. It is probably always incompatible with the perfect development of the faculties, and in the brains of those who have lived atrophy of certain parts, disappearance and calcification of nerve-cells, and degeneration of brain-fibers have been found on *post-mortem* examination.

Certain **heterotopic conditions**, by which gray matter in the form of streaks or scattered patches occurs irregularly scattered throughout the white matter of the cerebrum or cerebellum, appear to be congenital. They may have no clinical significance, but seem to be rather more frequent among epileptics and the insane than among normal persons.

CIRCULATORY DISTURBANCES OF THE BRAIN.

Anemia of the brain is characterized by a diminished quantity of blood in the vessels of the pia mater and by a pallor of the gray substance. In the white substance, when incised, there are fewer red dots where vessels are cut across than usual.

The condition is not frequent. It may occur in general anemia, especially that following hemorrhage, or may be a local process, sometimes collateral in origin—that is, resulting from the determination of blood to other parts or organs of the body, particularly the lungs and the abdominal organs. It may also result from spasmodic contraction of the blood vessels and from disease of the vessels, though it must be remembered that the free anastomoses of the vessels of the circle of Willis compensate for most irregularities of this kind. Collections of fluid in the ventricular cavity and in the subarachnoidean space may originate an ischemic condition by pressing the blood from the veins and interfering with the entrance of blood through the arteries.

Chronic anemic conditions, such as are seen in progressive pernicious anemia, marasmus, and cachexia, also occur. The anemia which depends upon vascular disease and obstruction must also be chronic. Stengel finds that in chronic anemia of the brain the organ is smaller and softer than normal. The ventricles are somewhat enlarged, the convolutions shrunken in appearance, and the sulci deeper than normal.

Ischemia of the brain is common from thrombosis and embolism. It is followed by softening and cyst formation.

Hyperemia.—Active Hyperemia.—In spite of its surrounding bony capsule—the skull—the brain tissue is subject to considerable variation in its contained blood. The blood-supply of the brain is increased during functional activity and diminished during rest. A pathologic hyperemia always accompanies inflammatory and toxic conditions, such as are seen in the infectious diseases, tetanus, rabies, sunstroke, meningitis, encephalitis, acute delirium, etc.

Local active hyperemia is seen in all cases of focal inflammatory conditions, or in cases of meningitis may occur in the brain substance immediately beneath the pia mater. It may also follow thrombosis with red softening of the brain tissue.

Passive hyperemia of the brain occurs in cardiac disease, pulmonary affections, etc., when the escape of blood from the cerebral veins is prevented, or when paralytic dilatation of the vessels causes an increase in the intracranial pressure. It may also be caused by tumors of the neck pressing upon the jugular veins. Brain tumors also sometimes cause hyperemia by pressing upon the veins of the brain (veins of Galen, etc.) and preventing the blood from escaping. Under such conditions the arteries continue to admit blood and the vascular tension within the skull is greatly increased.

Thrombosis of the sinuses of the dura mater also obstructs the escape of the blood from the brain and causes hyperemia.

The morbid anatomy of the lesion is very simple. The veins of the membranes, especially of the dura, are large and distended, those of the pia mater are unusually full of blood, and the brain appears larger, softer, and moister than normal. The color is also somewhat changed, the gray matter being of a slaty color and the white matter sometimes tinged with blue.

Local congestion is seen where the venous circulation is impeded because of thrombi, pressure from neoplasms, etc.

Edema of the brain occurs from a variety of causes, most of which bring about primary passive congestion to which the edema is secondary. In passive congestion there is but little doubt that an increased fluid transudate occurs. It is, however, speedily taken up by the lymphatics, so that the amount of cerebrospinal fluid is not markedly increased. When, however, the amount of transuded fluid is great or its escape through the lymphatics impeded, the fluid collects and edema results. The fluid is found chiefly in the subarachnoidean space. The membranes are elevated, the convolutions are indistinct, and a pearly luster is observed upon the surface of the brain.

The character of the fluid is different from that of the normal cerebrospinal fluid, being more frequently turbid and containing a greater amount of albumin. In nearly all cases of marked edema more or less well-marked evidences of inflammation can be observed in the form of proliferated endothelium of the arachnoid and round-cell infiltration about the blood vessels.

Edema occasionally results from intoxication, as in Bright's disease, etc. It may also be local in the neighborhood of softening.

In acute hydrocephalus fluid sometimes works its way into the white substance of the brain and penetrates as deeply as the internal capsule, where its pressure upon the motor fibers may be followed by transient hemiplegia.

Hemorrhage into the brain may be either *minute* (*punctate* or *punctiform*) or *massive*.

Minute hemorrhages of the brain may occur by diapedesis or by rhexis of the small blood vessels. They occur in nearly all cases of acute congestion, in all the inflammatory conditions of the brain, in a variety of specific infectious diseases, and in certain toxic affections, of which lead is probably the most important. In purpura, scurvy, small-pox, anthrax, and malaria such lesions are very frequent. Minute hemorrhages may also occur from arteriosclerosis.

Punctiform hemorrhages may be of microscopic size or the size of millet-seeds or even of peas. As a rule, however, it would be well to classify pea-sized hemorrhages among the massive hemorrhages, unless they were numerous. Minute hemorrhages seem to be most frequent in the gray matter of the brain, and they usually occur in the cerebral cortex. The escaped blood is partly infiltrated into the brain-substance and partly into the perivascular spaces.

The changes induced by the punctiform hemorrhages are, in general, similar to those seen following massive hemorrhages, but are so insignificant that they are usually unaccompanied by any obvious lesions.

Massive hemorrhages of the brain most frequently result from increased arterial pressure in vessels previously affected with arteriosclerosis. It usually affects the branches of the middle cerebral artery, which enter the anterior perforated space to be distributed to the basal ganglia. One of these arteries—that which distributes its ultimate branches to the lenticular nucleus—is more frequently affected than any other, and for this reason has been called by Charcot *the artery of cerebral hemorrhage.* Its rupture usually takes place in the internal capsule, or so near it that the escaping blood almost invariably presses upon or destroys its important fibers.

The branch to the optic thalamus is much less frequently affected, but occasionally ruptures. After the cerebral basal ganglia and important nerve-tracts, the pons is next most frequently affected. The cerebellum is sometimes the seat of hemorrhage; the medulla very rarely so.

Probably the cerebral cortex is the rarest seat of massive spontaneous hemorrhage, though in hemorrhage resulting from traumatic lesions of the skull cortical hemorrhage is to be expected.

Spontaneous hemorrhage nearly always follows the rupture of small aneurysms. In 77 cases which Charcot and his associates studied, the occurrence of aneurysms of this kind was invariable.

The effects of cerebral hemorrhage may be described as *primary* (*local* or *remote*) and *secondary*.

Primary Effects of Cerebral Hemorrhage.—The local effects may be described as immediate and late. The immediate result is the escape of blood into the brain-substance, which it tears apart and compresses. The result of this damage is the invariable establishment, should the patient live, of a series of retrogressive changes known as *softening*, which, in this case, because of the red color imparted to the softened mass by the escaped blood, is called *red softening*. Not long after the escape of the blood coagulation takes place, and a mass is formed which can be correctly spoken of as a *cerebral hematoma*. The surrounding healthy tissue, which is irritated by the coagulated blood and degenerated tissue, soon begins to protect itself by building about the clot a connective-tissue or neuroglia capsule which may more or less completely isolate it.

Up to this time the hemorrhagic area has been of a dark-red color, and soft and mushy in consistence. A hyperemic zone surrounds it, in which there may be punctiform hemorrhages.

The exact seat of hemorrhage will modify the macroscopic appearances, as will also the size and extent of the lesion; thus the hemorrhage may be small and distinctly local, or may be so large as to lacerate its way into a lateral ventricle and fill it, or, indeed, all the ventricles, with blood, and then, escaping through the transverse fissure, diffuse itself over the subarachnoid space. Again, when the hemorrhage is cortical, it may be subpial, or working its way through the pia, may appear in the subarachnoidean space.

As time passes the fluid part of the escaped blood is absorbed by the lymphatics, and the surrounding tissue becomes less compressed. The corpuscles being destroyed and their pigment separated in the form of hemosiderin, the area occupied by the clot becomes paler and of a rust color. Still later the destroyed nervous tissue, having undergone fatty metamorphosis, is absorbed and a more or less free cavity, described as an *apoplectic cyst*, is formed. This cyst has pigmented indurated walls, which probably consist essentially of newly formed glia tissue pigmented with hemosiderin in amorphous grains and darker amorphous and crystalline hematoidin.

The contents of the cyst consist of fragments of necrotic matter, crystals of cholesterin, and sometimes hematoidin. Old cysts may be full of a clear fluid containing a few crystals of cholesterin and hematoidin. In many cases, as the contents of the cyst are absorbed, the indurated walls contract, compressing the seat of disease more and more, until, in the place of the cyst, a scar is formed—*apoplectic scar*.

In the fresh hemorrhagic area, by carefully using a fine stream of water, the disintegrated tissue and blood may be washed away and the vessels exposed. Examination of these vessels with a hand lens or with the low power of a microscope will usually define the aneurysm from which the hemorrhage occurred.

The remote effects of cerebral hemorrhage are found in parts of the body that have been cut off from their centers of innervation by the tissue dissolution. The exact nature of these effects will vary according to the seat of hemorrhage, its size, and the kind of fibers or cells destroyed. Only an exact knowledge of the course of the fibers and an application of this knowledge to each case will enable the student to locate the seat of the lesion. Palsy, motor or sensory, or both, on the opposite side of the body is the usual outcome of the common form of cerebral apoplexy. The lesion in a considerable majority of cases is on the left side. The hemorrhage may be of sufficient size to produce the death of the patient in a short time. Indeed, sometimes it is so large and escapes with such violence as to cause almost complete destruction of a hemisphere of the brain. Such cases are rapidly fatal.

On the other hand, when the described absorptive changes occur, the condition of the patient gradually improves up to a certain point, beyond which it is impossible for him ever to advance, because the motor or sensory fibers are permanently destroyed.

The secondary effects of hemorrhage into the brain are *secondary degenerations*. These are all systemic, and affect different systems of nerves with each particular seat of the lesion. The usual lesion of cerebral hemorrhage being about the artery of the left lenticular nucleus and severing the motor fibers of the internal capsule, the most frequent form of secondary degeneration is that which, starting at the lesion, descends in the path of the pyramidal tracts. The entire pyramidal tract of one side may be destroyed. Any system of fibers may suffer degeneration after being interrupted, and the particular case that the student has before him must suggest the particular areas in which the degenerated fibers must be sought.

The secondary degeneration in the brain is similar to that seen in the spinal cord (*q. v.*), and is characterized by the same loss of the myelin sheaths, formation of compound granule cells, manifested by hyperplasia, loss of neuroglia, formation of corpora amylacea, etc. The ultimate outcome of the process is the loss of all nervous tissue and the survival of the neurogliar fibers only.

Thrombosis and Embolism of the Brain.—Thrombosis of the cerebral vessels may occur in consequence of endarteritis, embolism, etc. It is most frequent in embolism, and probably next most frequent in senile arteriosclerosis. The thrombi may form in any vessel in which the required conditions present themselves, the most frequent site probably being the basilar artery. The outcome of the process depends upon the position of the lesion and the ability of the collateral circulation to maintain nutrition. When the circulation fails, softening of the brain-substance—*encephalomalacia*—takes place.

Embolism of the brain most frequently depends upon verrucosities from the aortic valves in cases of endocarditis and dislodged fragments of thrombi. The emboli may enter and obstruct any of the cerebral vessels, though anatomic conditions usually determine that they take the most direct path from the heart to the brain, and in about 80 per cent. of the cases pass from the aorta into the left common carotid, the internal carotid, the middle cerebral artery, and then plug the artery of the Sylvian fissure. According to its size, the embolus may enter this vessel but a short distance or may penetrate to its finer branches. If the embolus lodges at the beginning of the artery of the Sylvian fissure, the resulting area of softening will embrace the corpus striatum, the internal capsule in large part, and the anterior part of the optic thalamus; if it enters the branch known as the arteria lenticulostriata, a cone-shaped area of tissue degenerates, its apex in the third segment of the lenticular nucleus and its body embracing the anterior two-thirds of the caudate nucleus and the internal capsule; if it enters the branch known as the lenticulo-optic artery, the damage occasioned is further back and embraces the posterior part of the lenticular nucleus, the internal capsule, the tail of the caudate nucleus, and the anterior part of the optic thalamus.

Sometimes the emboli are small enough to enter the vessels of the anterior perforated space. The resulting degenerations are then observed chiefly in the optic thalamus, and form areas varying in size from a pea to a marble.

Occlusion of the external posterior optic artery causes degeneration of the optic thalamus and of the peduncle of that side.

More rarely the emboli enter the anterior cerebral artery; still more rarely the posterior cerebral artery, usually reaching it through the vertebrals and basilar. It is interesting to note that of 131 cases of cerebral embolism studied anatomically by Gelpke, 64 (49 per cent.) were on the left side, 54 (41 per cent.) on the right side, and 13 (10 per cent.) on both sides.

The lodgement of an embolus is followed by thrombosis of the artery and almost at once by softening, as there are scarcely any collateral arterial branches.

Encephalomalacia.—Local softening of the brain results from ischemia. The most frequent causes are arteriosclerotic changes in the smaller vessels, thrombosis, and embolism, but such local areas are also sometimes seen in tuberculous meningitis in children, in meningitis, and in encephalitis. They may be due to capillary thrombosis or micro-organismal emboli. Traumatism also sometimes may cause encephalomalacia. The changes characterizing softening of the brain substance are necrotic, and belong in the class of *colliquation necroses*. It is customary to classify the lesions according to the color which the necrotic tissue presents. This, however, leads to the error of supposing that differences of color indicate differences of kind, whereas in truth they may simply indicate differences in the age or accidental additions of blood to the disintegrating mass. It is usual to speak of white, red, and yellow softening.

White Softening.—This is simple acute colliquation necrosis occurring in nervous tissue from which the blood-supply is completely and permanently shut off. The lesion forms a more or less distinctly circumscribed, larger or smaller area, in which the tissue rapidly disintegrates with the formation of a colorless, whitish, or grayish semifluid mass. When, in sectioning the brain, such a lesion is incised, the semifluid contents escape, leaving a cavity with ragged, ill-defined borders, and containing a reticulum composed of fine vessels and neuroglia fibers. If the escaped fluid be examined, it will be found to consist of remnants of destroyed nervous tissue, fragments of nerve-fibers with nodular and bulbous axis-cylinders, fat-drops, compound granule cells, leukocytes, and fibers and cells of the neuroglia—in short, all the elements resulting from destroyed nerve tissue.

Yellow softening differs from white softening in that there is more fatty metamorphosis and the softened matter contains yellowish pigment, which probably depends upon slight early admixture of blood. The softened areas are filled with material macroscopically resembling pus.

Yellow softening is not a specific process, but either a pigmented form of white softening or a late stage of the red softening.

Red softening is necrosis of the brain tissue with extravasation of blood. Its formation may be identical with hemorrhagic infarction, or there may be simple diapedesis of blood from a thrombus. The essential feature is that there shall be a sufficient admixture of red blood corpuscles to the degenerated mass to color it red or brown.

The encephalomalacic areas may be so small that they are scarcely discoverable to the naked eye, or they may be of considerable size. They may form rapidly when caused by thrombosis or embolism, very marked changes having been observed in some cases within forty-eight hours after embolism. When due to the gradually increasing obstructions of arteriosclerosis, they develop much more slowly.

In all forms it is probable that the sequence of events is much the same. The degeneration of the nervous tissue is accompanied by destruction of the myelin sheaths, formation of myelin drops, deformity and final destruction of axis-cylinders, formation of many fatty granules, corpora amylacea, collection of large numbers of compound granule cells, and the final formation of a cystic cavity filled with a mushy mass composed of these ingredients.

As time passes the elements undergo the most complete destruction and solution and are gradually absorbed, so that the original white, gray, yellow, or red contents give place to a slightly turbid fluid, or, indeed, in some cases, to a clear fluid. The cyst, which was at first very indistinctly circumscribed, now becomes definitely outlined and often has quite smooth walls, and may contain a delicate fibrillar reticulum. The lesion may remain such a smooth-walled cyst with clear fluid contents for years, or absorption and neuroglia proliferation may gradually transform the cyst into a scar. This change is probably more likely to occur when the softened area is subpial than when it is centrally situated in the brain. Subpial cysts may collapse, leaving depressed areas upon the surface of the brain, in which fluid from the subarachnoid space accumulates. The depressed area may have a yellow or brown color. The membranes adjacent alone may calcify.

About the fresher areas of softening a reactive hyperemia of mild grade, and occasional minute punctiform hemorrhages, may be observed. For quite a distance about the area the healthy tissue may be softer than normal.

When softening takes place in poorly vascularized portions of the brain, instead of a colliquation necrosis, a condition more analogous to coagulation necrosis is seen. It has been called by the French "*état criblé*." A condition possibly akin to this is sometimes seen upon the convolutions of the brain, and has received the name *plaques jaunes*. The affected areas are yellowish, firm, retracted, and covered by thickened pia with sclerotic vessels.

Though most frequent, as already mentioned, in the interior of the brain, the cerebral areas of softening may also at times affect the cortex, where considerable motor and sensory disturbance will result from the occasional destruction of the centers.

Encephalitis.—In discussing inflammation of the brain the same difficulty confronts us that was met with in connection with the spinal cord. The tissue of the nervous system is so peculiar, and above all so delicate, that the least deleterious influence is likely to cause an immediate degeneration of its elements, and in conditions that are certainly inflammatory, one is surprised to find degeneration or softening rather than conditions regarded as characteristic of inflammation. The ordinary criteria by which we diagnosticate inflammatory conditions are, therefore, absent in the nervous tissues.

1. **Traumatic Encephalitis.**—The traumatic form of inflammation is described first because its nature is unquestionable. It results from fracture of the skull with depression, laceration, and infection of the brain; from the passage of fire-arm projectiles, from punctures with sharp instruments, etc. Concussion of the brain from shock or blows produces changes that are properly included here. These changes consist chiefly of minute hemorrhages and local areas of encephalitis with subsequent sclerosis.

Traumatic Injuries without Infection.—These are interesting and significant. The tissue immediately acted upon by the object causing the lesion is usually occupied by a hemorrhagic extravasation, and is edematous and more or less comminuted. It undergoes a rapid and complete necrosis. Immediately surrounding the necrotic area is a zone of reaction resembling, though not identical with, similar conditions in other organs. In it there are hyperemia and perhaps punctiform hemorrhages, transmigration of leukocytes, and a tendency toward proliferation of the connective-tissue cells of the perivascular sheaths and sometimes of the neuroglia. This zone becomes deeply pigmented with hemosiderin if there has been much hemorrhage. The pia invariably takes part in this reactive process, and begins early to send in proliferating cells.

The nervous tissue in this zone of reaction behaves differently from other similarly situated tissues, for about the time that the reaction is established and regenerative efforts are apparent, it begins a typical softening. Cells and fibers melt away, the myelin sheaths breaking up into blocks, the cells becoming vacuolated, their processes short and nodose, fatty metamorphosis soon completely destroying them, and in a little while for a short distance in all directions there is complete destruction, characterized by tissue detritus, compound granule cells, etc.

As the patient's condition improves there is a removal of the necrotic and softened tissue, a connective-tissue and neurogliar hyperplasia, and a final, more or less complete, sclerosis or cicatrization. According to some observers, new nerve-fibers are seen extending through the new tissue, and karyokinesis of the nuclei of nearby nerve-cells suggests a tendency to regeneration. It is, however, improbable that any of the regenerative efforts succeed.

2. **Traumatic Injuries with Infection.**—When infection occurs in traumatic injuries of the brain, it usually affects the membranes of that organ rather than the nervous tissue proper,

and appears as a leptomeningitis which centers about the seat of injury. Meningitis under these conditions, as, indeed, under most others, is not limited to the pia, but involves the subjacent brain tissue, so that meningo-encephalitis is the more frequent lesion. The encephalitis which is thus produced is characterized by changes that are certainly inflammatory and others that are degenerative. In the pia mater and its prolongations, which accompany the blood vessels into the brain, considerable numbers of leukocytes collect, filling and distending the lymphatic spaces. Occasional leukocytes penetrate into the deeper part of the nervous tissue, but nearly always in the neighborhood of blood vessels. This tendency for the leukocytic infiltration to occur along the blood vessels and where the pial areolar tissue penetrates the brain has caused some writers to describe the condition as *interstitial encephalitis*. The brain-substance itself does not yield to the ready infiltration of leukocytes, but shows the effect of the inflammatory process by degenerative changes consisting of the disappearance of the cells of the pyramidal layers, the softening and reticulation of the tissue, the presence of compound granule cells, etc.

3. **Hematogenic Focal Encephalitis.**—This is probably the most frequent form of inflammation of the brain. It occurs in various infectious diseases, presumably from distribution of the specific micro-organisms through the circulation. It is not infrequent in pyemia, septicemia, acute rheumatism, typhoid fever, endocarditis, influenza, diphtheria, epidemic cerebrospinal meningitis, and scarlatina. It is sometimes seen in hydrophobia. The lesions may be very small, so as to be apparent only upon microscopic examination, or may be large enough to be distinctly visible to the naked eye. The larger superficial encephalitic areas usually project slightly above the surface of the organ, or when deep, are convex upon section, showing an increased condensation of tissue in the diseased area. There is also an alteration of color, the diseased tissue usually being bright red and almost hemorrhagic in appearance.

When examined microscopically, it is found that the blood vessels throughout the diseased area are distended, and interstitial hemorrhagic extravasations are frequent. The perivascular lymphatic vessels are full of outwandered leukocytes, and here and there are larger cells probably of endothelial origin. The nervous substance undergoes a rather rapid softening or degeneration. The ganglion-cells are destroyed, undergoing complete dissolution after a varying length of time; the fibers lose their myelin sheaths, which break up into myelin drops; the axis-cylinders become nodose, swell up, and undergo granular disintegration; the neuroglia-cells may degenerate, but often proliferate, especially at the edges of the diseased area and when the lesion is of some duration. There are usually compound granule-cells in abundance. Corpora amylacea may be found.

These areas usually progress to the stage of complete degeneration of the nervous tissue in their circumference, after which regeneration begins and slowly advances, with the ultimate formation of a scar of neuroglia fibers. Some few cases terminate by early resolution. Probably a majority of the cases with numerous or considerable sized lesions are fatal.

If the patient lives, it is not infrequent that the encephalitic areas go on to suppuration.

4. **Suppurative Encephalitis.**—This results from the operation of bacteria upon the nervous tissue. The bacteria most frequently found are the pneumococci, streptococci, and staphylococci. The micro-organisms may reach the brain *via* the circulating blood, or may enter it from diseased bones, especially the temporal bone in suppurative diseases of the ear. The outcome of the process is the formation of a true abscess, with all the characteristics of abscesses of other organs. There may be a single abscess or there may be several, depending upon the means by which the bacteria effected their entrance into the tissue. In hematogenous abscesses there are likely to be a number of abscesses; in direct extension, a single abscess.

The abscess may be as large as a hen's egg. Rarely such abscesses have been known to destroy nearly all the tissue of a hemisphere of the brain. As much as 400 c.c. of pus has formed in a single abscess of the brain. The abscess probably originates from a perivascular collection of cells which represents the focus of the inflammation. These cells receive continual reinforcements, and the collection increases in size. The surrounding nervous tissue readily degenerates as the abscess impinges upon it, and thus makes room for its growth. The contents of the abscess are usually creamy pus mixed with the débris of the nervous disintegration. When the activity of the inflammation subsides and the abscess ceases to increase in size, there forms about it a distinct wall of proliferated neurogliar fibers and cells. Whether or not the abscesses ever absorb or calcify is uncertain. Secondary degenerations commonly follow abscess formation with destruction of nerve-fibers.

The abscesses are most frequent in the cerebrum, about two-thirds of the cases occurring there. Most of the other cases affect the cerebellum, abscesses being rare in the pons and medulla. The size varies from a pin-head to an egg. The average size is about that of a walnut or hen's egg.

Occasionally the abscesses rupture upon the surface of the brain, with resulting suppurative leptomeningitis; sometimes they rupture into the ventricles of the brain and excite violent inflammatory reaction.

Very small abscesses sometimes resorb and heal, with the formation of fibrous scars. Large abscesses may go on to a fatal termination. After the acme of their growth has been passed, they often remain latent for many years and call attention to themselves, chiefly through secondary degenerations.

The brain tissue surrounding the abscess is usually edematous and softened. It may also be hyperemic.

Toxic Encephalitis.—In many of the infectious diseases and in various intoxications certain substances brought by the circulating blood act injuriously upon the nerve-cells, so as to bring about changes too fine in their nature to be discoverable without the use of the microscope and the most perfectly adapted methods of staining and examination. For want of a better heading under which to speak of them they are here grouped as toxic lesions.. Such changes are seen in diphtheria, tetanus, lead-poisoning, and to a less marked degree in alcoholism. The chief changes take place in the nerve-cells of both brain and spinal cord, and naturally vary somewhat according to the structure and complexity of the cells.

1. **Changes in the Configuration of the Cell.**—The normal ganglionic nerve-cell is irregular in shape and presents a variable number of rather short, thick processes, which branch rapidly until they form thickets of delicate branches (*dendrons*). From these branches there project in all directions minute, bristle-like, short offshoots termed *gemmules*. One of the cellular offshoots does not divide and is of uniform width. This is the *neuraxon*, or axis-cylinder process. At regular intervals along its course there are long, delicate, transverse offshoots, known as *collaterals*. The dendrons, gemmules, and collaterals can be properly studied only by the silver staining process of Golgi. In the toxic and infectious disorders under consideration the gemmules first disappear, next the dendrons become less numerous, short, and thick, and may disappear, leaving only a few branched twigs where a thicket should have existed. The collaterals of the neuraxon may be reduced in number or lost, and the axis-cylinder itself may present nodosities and varicosities along its length.

2. **Changes in the Protoplasm of the Cell.**—(*a*) *Vacuolation.*—The occurrence of a few vacuoles in the protoplasm of the nerve-cells may not necessarily indicate disease. In the conditions under consideration, however, vacuolation is frequent and may exist to an extreme degree. The vacuoles may be of immense size, and be filled with liquid in which filaments of fibrin (?) may be observed.

The vacuoles may not only be large, but may also be very numerous and of various sizes. What the vacuoles contain is a matter of some doubt. Some regard them as composed of lymph assumed by the cell, others as evidences of necrosis.

Sometimes a form of cellular degeneration, looked upon by von Recklinghausen as colloid, takes place and gives the cell the appearance of containing vacuoles.

(*b*) *Pigmentation of the Cytoplasm.*—Degenerative changes of the cytoplasm are very commonly associated with the occurrence of pigmentary changes. The cells contain scattered yellowish-brown granules which are of small size, but which may collect to form masses representing the cells when their destruction is complete. The formation of these pigment-granules occurs hand in hand with the destruction of the chromatophilic bodies of the cell.

Pigmentary changes are usual in senility, but may be expected in all the cellular degenerations.

(*c*) *Changes in the Chromatophilic Bodies.*—When the tissue is stained by Nissl's method or any modification of it, the normal ganglionic cells are found to contain a good many chromatophylic granules—coarse; rather elongate or spindle-shaped granules, with a decided affinity for the stain. These granules usually have a concentric arrangement about the nucleus, but in the outer rows they sometimes change their positions when in relation to the processes of the cell toward which they are deflected and into which they sometimes extend. The nature and function of these bodies are unknown. Between them the cytoplasm is transparent and clean. When the cells are acted upon by any injurious agent, one of the first changes observed takes places in the chromatophilic granules, the normal relations of which are disturbed, so that they become irregularly scattered throughout the protoplasm of the cell. They diminish in size and in number, and may disappear from the cell altogether. They sometimes appear to be enlarged, and mass themselves together irregularly. Sometimes the granules dissolve in the cytoplasm and impart to it a peculiar staining quality by which the whole cell stains diffusely and deeply (*pyknomorphous condition*).

(*d*) *Nuclear Degeneration.*—The nucleus may show the first signs of retrogressive change. It may become vacuolated, or may be paler than normal. Sometimes its sharpness of outline entirely disappears and it becomes indefinite or spinous. The excessive vacuolation that sometimes occurs has been compared to the morula stage of the segmentation of the ovum.

The staining quality of the nucleus next alters. Instead of the sharp, clear chromatic threads, indefinite accumulations are found lying well toward the periphery of the organ. Vacuoles form in the nucleus in the last stages of its existence.

Not only does the nucleus degenerate, but it also becomes dislocated in degenerated cells. Instead of a nearly central position in the cell, it is peripheral, and may cause bulging of the cell surface. It is even claimed by some observers that the nucleus may escape from the cell. The dislocation of the nucleus is thought to depend upon the occurrence of large vacuoles in the protoplasm, which crowd it out. Ultimately the karyolysis goes on to the complete destruction and disappearance of the nucleus.

Chronic encephalitis or **sclerosis** is seen in all cases of injury to the brain followed by recovery. It occurs after traumatic lesions, after focal necrosis, after hemorrhage, after abscess, and in the chronic specific inflammations. Sometimes it occurs as an independent idiopathic affection. When disseminated patches of sclerosis are found in the brain, it is difficult to determine whether they originated as such or had their inception in inflammatory or infectious lesions, followed by organization and sclerosis.

Multiple Localized Sclerosis.—This condition is analogous to the multiple sclerosis of the spinal cord, and is characterized by the formation of irregularly scattered foci in which signs of degeneration, with subsequent neurogliar hyperplasia, appear. The softening may precede or accompany the sclerosis. The different lesions may be of various ages. They occur in both the gray and the white substance, and may be few or many. They vary greatly in size, and are irregular in shape, though sharply defined.

When superficial, they may be recognized by the naked eye as areas of a grayish or pinkish color. To the touch they are slightly indurated. Upon microscopic examination one finds that the nerve-cells show signs of retrogressive changes, from the mildest variation from the normal to complete dissolution. The nerve-fibers lose their myelin sheaths and become bulbous or are destroyed. Myelin drops, compound granule cells, free fat molecules, occasional leukocytes, corpora amylacea, and unrecognizable molecular matter are present. The sclerotic changes consist in the formation of hyperplastic coarse neurogliar fibers and numerous cells. Occasionally nerve-fibers without signs of degeneration pass through the lesion. These are thought by some to be *regenerated fibers*.

Diffuse Sclerosis.—This differs from the multiple scleroses in that it affects wide-spread areas of the brain-substance. It probably does not often result from toxic or inflammatory conditions, but bears some relation to the development of the brain tissues. The lesion may be general and lead to an apparent hypertrophy of the brain in children. It is more frequently rather circumscribed, and may be with difficulty differentiated from glioma. In the course of time the apparently hypertrophied tissue becomes smaller through atrophy of the nervous elements, and the sclerosis is more apparent in consequence.

The diffuse sclerosis is apt to affect lobes of the brain or groups of convolutions in the distribution of a certain blood vessel. It is usual for it to result in atrophy. The convolutions appear to be reduced in size, and the fissures broader. The pia is usually adherent, and the tissue indurated and almost cartilaginous.

The microscopic features are loss of nervous substance with marked proliferation of the neurogliar tissue.

The cause of the trouble is obscure. Its relation to the blood vessels suggests that during embryonal development vascular disturbances or irregularities have occurred. In this form of sclerosis there are always marked degenerations.

Tuberculosis of the brain may be primary and hematogenic, or secondary and lymphogenic in origin. The secondary cases, for the most part, succeed tuberculosis of the membranes.

Most tuberculous lesions of the brain begin in the pia and its vessels and extend to the brain tissue. In nearly all well-marked cases of tuberculous meningitis the brain substance is involved in this way, the tubercles being distributed along the perivascular tissues. Even in cases of primary tuberculosis of the brain substance the extension of the disease seems to select by preference the superficial portions of the organ and extend along the perivascular connective tissue. Miliary tubercles are frequent upon the small vessels of the anterior and posterior perforated spaces.

Primary tubercles of the brain are usually single. Their distribution is irregular and they remain local, gradually increasing until large, cheesy masses, which sometimes become as large as a goose-egg, are formed. The masses are usually of dense structure, yellowish-white in color, and are surrounded by a granulation-tissue zone. Sometimes the tubercles calcify. sometimes they soften and contain greenish-yellow, puriform matter. The masses, when large, are spoken of as *tyromata*. They are composed of aggregations of tubercles which continually grow by the addition of fresh tubercles from the granulation-tissue zone that is constantly being newly infected so long as the mass is active in its growth.

Syphilis of the Brain.—The chief syphilitic lesion is the gumma. which usually springs from the pia and extends to the brain. The gumma appears as a grayish or reddish-gray, irregularly shaped, translucent mass. It rapidly undergoes coagulation necrosis and softens or caseates. When recovery occurs, it is with the formation of dense cicatrices.

Syphilitic endarteritis is very frequent in the blood vessels of the brain. The circulatory obstruction to which it leads is a frequent cause of local softening—*syphilitic encephalitis.*

Actinomycosis of the brain is rare, but may occur in infection of the tissues of the neck and throat, permitting the entrance of the microorganism into some of the openings of the skull. The pia is usually the seat of a purulent leptomeningitis, with minute nodules of granulation tissue which sometimes extend into the brain substance. Primary actinomycotic nodules of considerable size are rarely observed.

Tumors of the Brain.—Glioma.—Glioma is the most frequent tumor of the nervous tissue. It is most commonly seen in the cerebral hemispheres, but occurs also in the cerebellum, upon the pons, in the medulla, and in the spinal cord. It may also occur in the eye and in the various nervous ganglia.

Glioma of the brain is said by Stroebe never to spring from or invade the pia mater. Ziegler, however, states that when it extends to the pia, it sometimes induces connective-tissue proliferation. The tumor usually produces no visible external alteration unless it occurs in the medulla or pons, which may be enlarged by its presence. In the cerebrum its presence is not indicated by any change of external appearance. The pia over the seat of tumor is also very rarely altered in appearance or quality. Upon section of the brain, however, the glioma appears as a red, reddish-gray, grayish, or yellowish area, which infiltrates in all directions and gradually fades away into the surrounding healthy tissue at its borders. Its substance is usually firm, but may be soft if myxomatous degeneration is present; or may be telangiectatic, cavernous, or cystic, the cysts resulting from softening. When vascular, it is red proportionately to the vessels it contains. Hemorrhagic areas appear dark red in color. The tumor arises from the neurogliar tissue and grows by infiltration. At its oldest, most central part no nerve tissue is present, while at its infiltrating edges there is a free admixture of neuroglia and nerve tissue.

Microscopically the glioma consists of neuroglia cells with their interlacing protoplasmic offshoots which make up the matrix of the growth. There are usually many blood vessels and capillaries. An occasional medullated nerve-fiber is found in the tumor, especially at the edges. In some gliomata are to be found groups of ganglionic nerve-cells or scattered ganglionic cells with branched processes and sometimes two or even more nuclei. Gliomata of this structure are sometimes called *ganglionar neurogliomata.* They are supposed by Ziegler to depend upon accidents of embryonal development. They may present the usual uncircumscribed appearance or may be more distinctly nodular. The color may be homogeneously white, grayish white, or mixed white and gray. The tumor is less likely to be vascular and red than the glioma itself.

In glioma the blood vessels very frequently show hyaline thickenings and sometimes present fibrous enlargement of the adventitia. The preëxistent nerve-cells and fibers of the invaded areas degenerate and disappear, sometimes, however, being retained for a long time.

Some gliomata present a sarcomatous appearance and are described as *gliosarcoma.* Presuming that glia is of epiblastic origin, it is difficult to conceive of such a combination. If by the term be meant that the glioma has an unusually rapid infiltrating nature, it would be better to adopt the term suggested by Ziegler and call it *medullary glioma.* A true gliosarcoma could result only from the growth within a glioma of cells derived from the perivascular connective tissue. This must be very rare.

Sarcoma of the brain is not uncommon. It usually arises from the pia mater or from the connective tissue of the vascular sheaths, and forms distinct nodes which are rather sharply circumscribed and not infrequently encapsulated. A surrounding zone of edematous and softened brain tissue makes it very easy to remove them from their nidus. They cause extensive secondary degenerations. When large, they may project slightly from the surface of the brain and sometimes present umbilications. The pia is nearly always involved or invaded.

The *small round-cell sarcoma* is the most frequent form, though spindle-cell and irregular-cell sarcomata also occur. Giant-cells are not uncommon in sarcoma of the brain. The tumors are frequently divided by fibrous partitions and may be alveolar. *Angiosarcoma* is common, and the form known as *perithelioma* or *myxangiosarcoma tubulare* is of frequent occurrence.

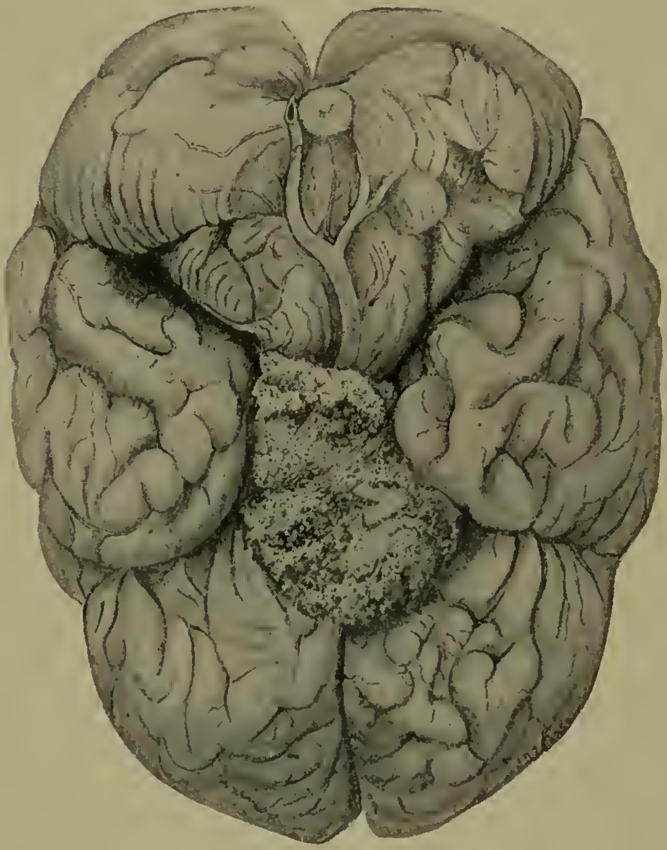

FIG. 309.—Angiosarcoma of the pituitary body.

On section, the tumors are somewhat yellowish or grayish in color, and may be mottled by hemorrhages. The sarcoma is a tumor of childhood or early adult life, and is more common in the cerebral cortex than elsewhere. Calcification in sarcoma of the brain probably causes the formation of *psammoma* or *psammosarcoma*.

Endothelioma in the brain sometimes develops from the pia, sometimes from the choroid plexuses.

Psammoma is most frequently found in connection with the choroid plexuses and the membranes of the brain. They are usually small, rarely larger than a cherry, and gritty and rough on section.

Fibroma of the brain grows from the membranes and from the perivascular connective tissue, and is of rare occurrence. It is usually seen in the hemispheres. It may be hard and fibrous.

Angioma of the brain is a rare, usually congenital tumor. It resembles somewhat an acute inflammatory area, appearing like diffuse red blushes. Sometimes, when cavernous, the color is dark red or purplish. These tumors consist of groups of telangiectatic blood vessels which have induced softening of the surrounding brain tissue as they enlarge, or if congenital, have caused atrophy of the brain tissue.

Lymphangioma is also rare and originates chiefly from the pia.

Lipoma of the central nervous system is very rare and probably always indicates a developmental defect. It is usually found where such defects are likely to occur—that is, in the neighborhood of the hypophysis cerebri and cauda equina.

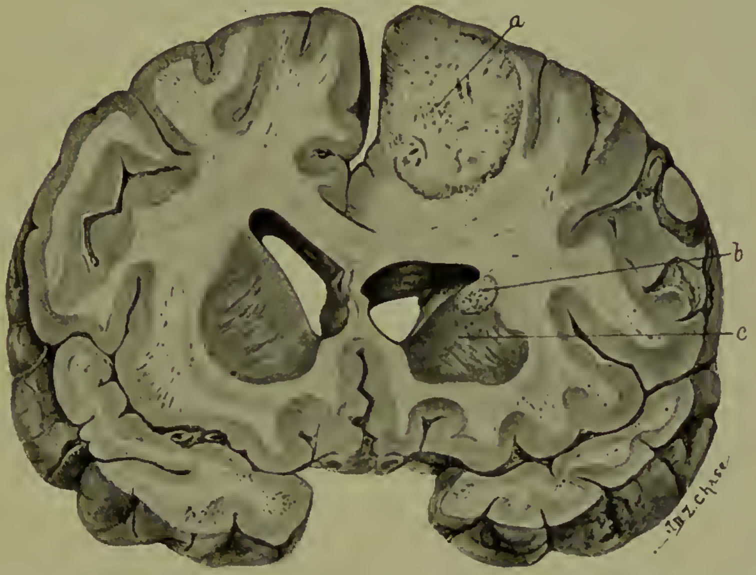

FIG. 310.—Secondary carcinoma of the cerebrum. The organ is cut transversely and vertically through the optic thalamus: *a* and *b*, Tumor masses; *c*, optic thalamus

Osteoma in the brain may originate from the bones or from the membranes, osteophytes of the falx cerebri being frequent.

Secondary tumors of the brain, both sarcoma and carcinoma, are of embolic origin and are not infrequent.

Parasites of the brain are rare. The echinococcus cysts and the Cysticercus cellulosæ have occasionally been observed.

THE EPIPHYSIS CEREBRI, OR PINEAL GLAND.

This little body projects into the transverse fissure of the brain and is in relation with the corpora quadrigemina. It is, however, entirely surrounded by pia mater. It develops from the anterior cerebral vesicle, projecting from its roof at the extreme posterior portion.

The organ consists chiefly of connective tissue with closely approximated rounded spaces of small size, occupied by epithelial cells, some of which are round, some elongate, and provided with projecting processes. It is rich in vessels contains some nerve-fibers, probably belonging to the sympathetic system, and always contains peculiar concentric mineral particles of *acervulin*, or *brain-sand*.

When the brain-sand increases beyond the normal, the pineal gland enlarges and is sometimes transformed into a *psammoma*. This name should, of course, be restricted to a tumor in the gland.

Diseased conditions of the pineal gland are rare. The organ sometimes appears congested, may be cystic, and is said to have contained adenomatous (?) growths. *Sarcoma* of the pineal gland has been observed. The blood vessels are not infrequently hyaline.

THE PERIPHERAL NERVES.

Anemia of a nerve-trunk could scarcely be recognized, as the nerves normally appear bloodless and white.

Hyperemia of the nerves is common, and can be recognized by redness and infection of the tissue and by swelling. Hyperemia is seen in traumatic, toxic, and infectious conditions.

Hemorrhages into the nerves are occasionally seen, usually in the form of minute, punctate extravasations in the endoneurium and perineurium. They occur in traumatism and infection.

Edema is rarely observed in the nerves. It occurs in inflammation.

Atrophy of the peripheral nerves results from pressure, as when neoplasms, etc., are in contact with and compress them. It may also result from inflammation and from loss of either the central connection or peripheral terminations, both of which conditions, by preventing the exercise of function, lead to atrophy. Atrophy may also be of senile origin.

The atrophy may occur very gradually, with loss of the myelin-sheaths and subsequently of the axis-cylinders, or may be a more rapid degenerative change, accompanied by fatty metamorphosis and later absorption of the myelin-sheaths. Amyloid bodies are of frequent occurrence in the diseased nerves. Birch-Hirschfeld points out that if the nerve be not universally affected by the retrogressive change, the atrophic fibers are invariably situated at the periphery, leaving the center of the nerve normal.

Degeneration of the nerves, like degenerations of the brain and spinal cord, cannot be sharply differentiated from inflammation, for degeneration always follows inflammation, and inflammatory changes not infrequently succeed degenerative ones. Cases of degeneration which are certainly not of inflammatory origin are called *simple degenerations;* others, *inflammatory degenerations.* The inflammatory degenerations are also described as *parenchymatous neuritis,* in contradistinction to *interstitial neuritis,* which affects the endoneurium and perineurium.

Etiology.—Degeneration of the nerves results from mechanical trauma, such as section, crushing, laceration, compression, diseases of the central nervous system with descending degeneration, poliomyelitis anterior acuta, and other conditions which sever the continuity of conduction from the ganglion cell to its ultimate termination.

Degeneration of the nerves also results from the infectious diseases, such as syphilis, beri-beri, typhoid, typhus, variola, diphtheria, scarlatina, influenza, etc. ; from intoxications of various kinds, as alcohol, lead, mercury, etc. ; and from circulatory irregularities, such as anemia.

The infectious and toxic substances usually operate upon the nerves generally, though some of them are selective and chiefly affect nerves contiguous to the local lesion, as in diphtheria, when the pharynx is likely to be most affected, or certain sets of nerves, as in lead-poisoning, in which the nerves supplying the extensor muscles of the forearm suffer most. Syphilitic nerve degeneration is probably best illustrated in tabes dorsalis.

The **morbid changes** come on very rapidly in acute cases, and in experimental conditions, in which the nerves are intentionally disturbed, the earliest changes may be observed on the first day. The myelin-sheaths are observed to be clouded in appearance, and the formation of blocks or drops of myelin substance begins. A few days subsequently large myelin drops are formed, fatty degeneration is in progress, and leukocytes are busy carrying away the fatty molecules. The axis-cylinders retain their vitality much longer than other parts of the nerve, but later become vacuolated and seem to crumble away. In severed nerves the degeneration is more rapid and more complete in the distal than in the proximal end. In the latter, the degeneration usually ascends to about the first node of Ranvier, where it ceases, or beyond which it does not pass for a long time. A few fibers of the nerve may degenerate all the way to the spinal cord.

Neuritis.—True inflammatory disturbances occur in the nerves as a result of traumatic injuries, such as laceration or crushing. They may also develop in consequence of hematogenous influences, such as intoxication by lead; or of infection, as in rheumatism, beri-beri, etc. The lesion can sometimes be recognized by the naked eye, as the nerve may be pinkish, swollen, edematous, hyperemic, injected, and showing hemorrhagic areas or foci of suppuration. Acute neuritis may also occur from the extension of inflammation from the surrounding tissues to the nerve.

The condition is essentially interstitial, and the chief changes are observed in the endoneurium and perineurium, in which the exudates are collected. The disease rarely progresses very far before the nerve-fibers undergo degeneration, with the usual characteristic appearances.

Microscopically, the connective tissue of the nerve presents the signs of inflammatory edema and congestion, with extensive round-cell infiltration and nerve-fiber degeneration. When the activity of the inflammation causes actual suppuration, the condition is sometimes described as *suppurative neuritis*. It is usually secondary to other serious pyogenic infection. Neuritis, according to its origin, may affect a single nerve or a number of them. In the latter case it is sometimes called *polyneuritis*.

Chronic neuritis is always interstitial, and may follow the acute form. It is characterized by a cicatricial hyperplasia of the connective tissue of the nerve, leading to gradual atrophy of the nerve-fibers. It is often called (after Déjérine) *chronic hypertrophic neuritis* or *proliferative neuritis*, in consequence of the new formation of connective tissue. It leads to complete disappearance of the nerve-fibers.

When the tissue is examined microscopically, the hyperplastic connective tissue is rather striking. It is rich in nuclei, and contains a good many small round-cells. Chronic interstitial neuritis is a possible cause of the progressive muscular atrophy.

Not infrequently the changes in the nerves are accompanied by or associated with ascending degeneration in the posterior columns of the cord, and sometimes with alterations in the ganglionic cells of the gray matter of the cord.

Tuberculosis of the nerves is probably always secondary, and depends upon the extension to the nerves of tuberculous disease in the membranes of the brain and spinal cord, from the bones, or from tuberculous lymphatic glands. The process is an interstitial inflammatory one, and leads to the formation of tuberculous granulation tissue in the connective tissue of the nerve, and later to the formation of cheesy masses. Secondary degenerations occur in the nerve, and remote effects may be observed in its distribution.

Syphilis of the nerves usually follows syphilitic disease of the membranes of the brain and cord, and exerts its effects chiefly upon the nerve-roots. The early effects observed consist of a marked cellular infiltration, which later gives place to extensive connective-tissue proliferation, succeeded by atrophy, degeneration, palsy, etc.

Sometimes syphilitic diseases of the arteries of the nerves obliterates or partially obstructs them, bringing about degenerative changes in their distribution and leading to various secondary changes.

Gumma of the nerves is rare, but has been observed in the cranial nerves. Nerves passing through gummata are destroyed.

Leprosy has a peculiar form known as *lepra nervorum,* in which lesions of the nerves are characteristic and constant, and lead to the anesthetic changes characteristic of the disease. The lesions depend upon the development of the bacillary nodes in the nerve-fibers, and an accompanying cellular infiltration, connective-tissue induration, and subsequent degeneration of the nerves, with connective-tissue proliferations in the form of spindle-like enlargements. The chief characteristic of the disease is the presence of large numbers of lepra bacilli, which can be observed in the tissue—some free and some in the cells.

Tumors of the Nerves.—**Neuroma** (*q. v.*) is the most frequent tumor of the nerves. *False neuroma* is more frequent than true neuroma, and may result from the growth in the connective tissue of the nerve of what would elsewhere be a fibroma, myxoma, or sarcoma. Such growths usually form small rounded tumors, which are often multiple.

The *plexiform neuroma* consists of connective-tissue enlargements that are more or less connected. It is possible that in these tumors some newly formed nerve-fibers are present.

Amputation neuromata form upon the ends of severed nerves, probably because of regenerative efforts, and consist of newly formed fibers with and without myelin-sheaths.

Neurofibroma is a tumor thought to develop from a combined outgrowth of the endoneurium and perineurium and the nerve-fibers.

Sarcoma of the nerves, sometimes called *malignant neuroma* or *neurosarcoma,* is of rare occurrence. It probably develops from the connective tissue of the sheaths of the nerves.

CHAPTER IX.

DISEASES OF THE REPRODUCTIVE SYSTEM.

DISEASES OF THE MALE ORGANS OF GENERATION.

THE PENIS.

Congenital Malformations of the Penis.—Total absence of the penis is very rare. Hypoplasia of the penis is characterized by a diminutive size of the organ, more closely approximating that of the clitoris. Double penis and penes with double canals, one urethral and one genital, are also very rare. The most frequent malformations result from imperfect fusion of the lateral halves and produce anterior or posterior insufficiency of the urethra. The more frequent of these is known as *hypospadia*, and is characterized by division of the urethra posteriorly, sometimes extending as far back as the root of the penis, sometimes as far as the perineum, the cleft dividing even the scrotum. The opposite condition, in which the urethra is not closed along the dorsum of the penis, is known as *epispadias*. It is not uncommonly associated with *extrophy of the bladder* and other deformities.

The prepuce is commonly abnormally elongated and constricted at the orifice, so that its retraction over the glans penis is impossible. This is described as *phimosis*. Sometimes the prepuce is very small or is not infrequently absent.

Inflammation of the penis usually affects the glans and prepuce. Inflammation of the glans is described as *balanitis ;* that of the prepuce as *posthitis ;* of both glans and prepuce as *balanoposthitis*. These inflammations result from traumatism and infection. They may depend upon decomposition of smegma, as well as upon the retention of ammoniacal urine beneath the prepuce in cases of phimosis. In rare cases of phimosis the retention of smegma, salts of the urine, desquamated epithelium, etc., beneath the prepuce may cause the formation of concretions or *preputial calculi*. The most frequent cause of these inflammations is venereal disease, especially gonorrhea and chancroid. Mycotic inflammations are occasionally seen beneath the prepuce, Friedreich having observed an aspergillus inflammation in this location.

The swelling of the prepuce in posthitis not infrequently produces an inflammatory phimosis and retraction of the prepuce, which, when swollen, is sometimes caught behind the glans. This is called *paraphimosis*, and by tight constriction of the tissues behind the glans may lead to serious secondary complications.

Traumatic injuries of the body of the penis, affecting the corpora cavernosa, are not infrequent. They usually cause preputial hemorrhage and heal with extensive cicatrices. When accidentally infected, suppuration and gangrene may occur.

Calcification of the tissue of the corpus cavernosum sometimes occurs. It may lead to true bone-formation.

Tuberculosis of the penis is very rare. It usually affects the glans, and is characterized by the formation of tubercles and ulcers, with cicatrization and necrosis. Sometimes the lesions resemble those of lupus vulgaris.

Syphilis.—The primary lesion, the true *chancre*, commonly occurs upon the penis. It may safely be stated that it is not always possible to recognize the initial lesion with certainty. The chancre usually heals with more or less cicatrization and leaves a permanent scar. It may be situated upon the glans at the corona, or upon the prepuce. Mucous patches may also be situated about the corona and beneath the prepuce in the secondary stage of syphilis (see Chancre).

Tumors of the penis are not uncommon, epithelial tumors being most frequent. *Hard papilloma* and squamous epithelioma are most common. The former usually arises from the corona, and forms a nodular or cauliflower-like growth which may attain a considerable size. The *epithelioma* usually arises from the surface epithelium of the prepuce or glans, but sometimes originates in the urethra. It forms a more or less warty and ulcerated enlargement, with metastasis to the inguinal glands. *Sarcoma* of the penis is occasionally seen and is rarely melanotic. *Angioma*, *lipoma*, and tumors formed by proliferation of the sebaceous glands are of rare occurrence.

DISEASES OF THE SCROTUM.

The scrotum is occasionally divided along the line of the raphé in cases of hypospadia.

Elephantiasis is of frequent occurrence in the subcutaneous tissue, and may cause the organ to form a pendulous mass nearly reaching the ground as the patient stands, and almost as large as his body.

Dermoid tumors are not infrequent in the scrotum, most of them probably being inclusion cysts.

Epithelioma of the scrotum is said to be common among chimney-sweeps and paraffin workers.

DISEASES OF THE PROSTATE GLAND.

The prostate gland is a fibromuscular organ, the homologue of the uterus. It is situated about the neck of the bladder, and perforated by the urethra, into which its numerous branched tubular glands empty. The organ is very small in childhood, takes on a considerable development at puberty, and undergoes a healthy atrophy, more or less marked in old age.

Atrophy of the prostate rarely occurs in youth or middle life, but is common in advanced years. It affects both the glands and their matrix, the epithelial cells undergoing fatty metamorphosis and largely disappearing. It is said that atrophy of the prostate may be a cause of sterility. The organ appears unusually small, and contains dilated and cavernous glandular spaces.

Hypertrophy of the Prostate.—Enlargement of the prostate is a very common disease of old men. The enlargement may depend upon a true hypertrophy of the whole organ or of one of its lobes.

The enlarged prostate may be characteristic in appearance and at once indicate the nature of the affection. Thus, if it appear homogeneous, as is normal, the enlargement probably depends upon hypertrophy or hyperplasia. If there are nodular masses in its structure, it is more probable that neoplasms are present. The microscopic appearances may, however, be somewhat confusing, as it is not always possible positively to differentiate between glandular hyperplasia and adenoma.

The organ is not uniformly affected, but presents unilateral or median enlargements, depending upon overgrowth of particular lobes. Of these, the median enlargements are clinically the more important, because of the greater interference which they occasion with urination. The enlarged median or posterior lobe may form a body as large as a cherry or walnut, obstructing the urethral orifice and making entrance of urine into the urethra very difficult.

Enlargements depending upon simple hypertrophy are probably rare, while those depending upon glandular and interstitial hyperplasias are very common. Of the latter, the glandular hyperplasia closely simulates adenoma, and microscopically presents beautiful acini with columnar epithelial cells. The interstitial hyperplasia is characterized by increase of the fibromuscular tissue of the matrix, and may be accompanied by an actual atrophy of the glands, which appear as widely scattered tubules with atrophic cells.

Inflammation of the prostate—prostatitis—is nearly always of secondary origin. It occurs from infection from the urethra in cases of gonorrheal urethritis; from infection from the bladder in cases of cystitis with decomposition of the urine; from lymphogenic infection in cases of proctitis and pelvic cellulitis; and in rare cases from hematogenous infection by pyogenic bacteria circulating in the blood.

The inflammations are, for the most part, acute, and will vary in appearance according to the particular mode of infection. Thus, in the infection that takes place through the ducts in urethritis and cystitis, the brunt of the inflammation falls upon the tubules of the gland and produces a catarrh, with accumulations of pus in the tubules, desquamation of cells, round-cell infiltrations of the peri-alveolar tissue, and a subsequent series of atrophic changes in cases which do not undergo a ready recovery by resorption.

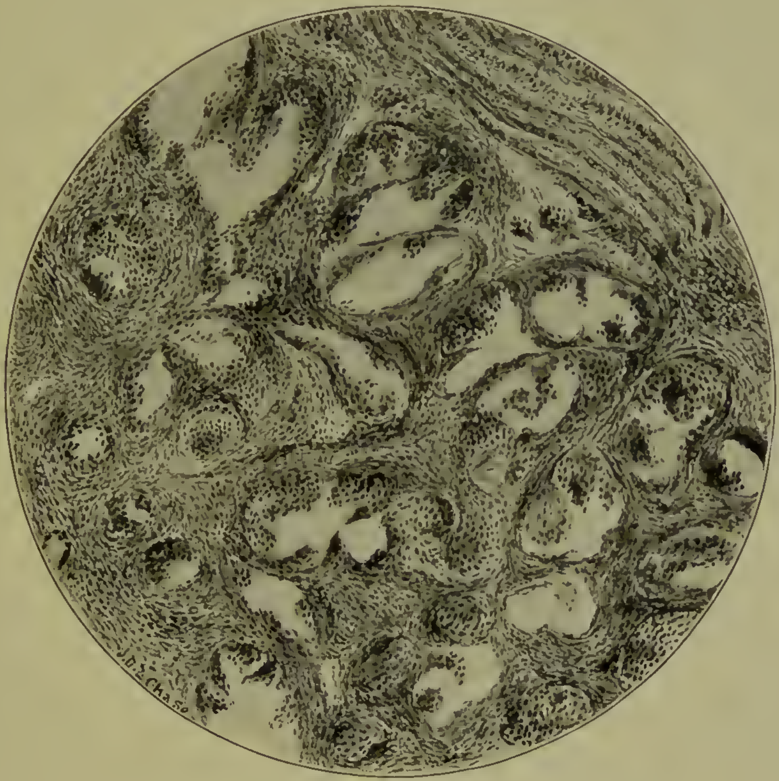

FIG. 311.—Hypertrophy of the prostate gland.

The lymphogenic and hematogenic infections occasion interstitial inflammations which usually take the form of abscesses of varying size, some being no larger than a pea, others as large as a walnut. They may heal by absorption or may become encapsulated and calcified, or they may rupture and evacuate. Rupture may take place into the urethra or the periprostatic cellular tissue. Urethral and vesical evacuation is quite frequently followed by infiltration of the tissue by urine, further infection, phlegmonous inflammations, and the formation of larger pus collections, which point at remote parts. When such untoward results do not take place, the abscess usually heals kindly and cicatrizes.

Tuberculosis of the prostate is usually secondary to tuberculosis of the testicle, seminal vesicles, etc., and occurs by lymphatic distribution. In rare cases of hematogenic origin the disease is primary in the prostate. The tubercles may form large, cheesy masses, which may become encapsulated or calcified, or may soften and rupture, discharging the infectious contents into the surrounding tissue and provoking a wide-spread lymphogenic tuberculosis.

Tumors of the prostate are not common. That most frequently observed is a fibromyoma that resembles the uterine fibroid. The tumor occurs in the form of more or less circumscribed nodes which distort the organ. Sometimes glandular elements are observed in these tumors.

Sarcoma and **adenoma** are rare tumors of the prostate.

Carcinoma of the prostate is not rare, and occurs as a nodular, yellowish-white mass, which projects into the urethra and neck of the bladder, soon becomes ulcerated, and forms deep, ragged excavations. The disease early gives metastasis to the inguinal glands. The growth develops from the glandular cells of the acini of the organ, which form cylindric, elongate, cellular masses, with branched extensions and occasional large cell-nests. The interstitial tissue may be unchanged or may be very rich in cells, and apparently in active proliferation.

The tumor invades the neck of the bladder, seminal vesicles, and rectum by continuity of tissue, gives metastasis to remote organs, and is rapidly fatal.

Cysts of the Prostate.—Rarely, cysts are formed in the prostate by obstruction of the ducts and retention of the secretions. Cystic dilatation of remnants of Müller's duct may also occur. The vesicula prostatica is a persistent remnant of Müller's duct, and forms a pocket which sometimes becomes quite widely dilated. It is not pathologic except when widely dilated.

Parasites of the prostate are very rare. Echinococcus cysts have been observed.

Calculus in the Prostate.—Occasionally grains of urinary gravel passing through the urethra enter and remain in the prostatic ducts. These are sometimes incorrectly described as prostatic calculi.

Concretions commonly form in the prostatic alveoli, especially in old men. They may be discovered only by microscopic examination, appearing as rounded or oval, colorless, translucent, smooth, concentric bodies. They are often described us *corpora amylacea*, and in composition seem related to the amyloid substance, striking a blue or mahogany-brown color with iodin and potassium iodid solutions, though sometimes they fail to react. As they become larger they appear of a yellowish, brownish, or blackish color, and receive incrustations of phosphatic salts and oxalate of calcium. At this stage the bodies become visible to the naked eye, and grit upon the knife when sections of the gland are made. They may become so large as to fill up and dilate the ducts, even projecting into the urethra and interfering with the passage of urine, by which they may be washed out and escape through the urethra.

Diseases of Cowper's Glands.—These small glands, one on each side, situated in the membranous portion of the urethra, just behind the bulb of the corpus cavernosum, are sometimes infected from the urethra and sometimes invaded by neoplasms, etc.

Inflammation.—Inflammation usually occurs in inflammation of the prostate and in all forms of urethritis. The glands become large and hyperemic, and may suppurate. In the latter case they evacuate into the urethra. If they rupture externally, fistula occurs. Chronic inflammation leads to permanent enlargement with narrowing of the urethra.

Cysts.—Retention cysts of Cowper's glands are not infrequent.

THE SEMINAL VESICLES.

Vesiculitis, or inflammation of the seminal vesicles, is caused by infection from the urethra in urethritis,—gonorrhea,—or is conveyed from the vas deferens in primary suppuration of the epididymis. It may also occur in consequence of prostatitis. The inflammation is catarrhal, the seminal vesicles being little more than the expanded tortuous upper extremity of the vas deferens. When inflamed, their tubules are filled with a mucopurulent secretion impoverished in spermatozoa. The organs are enlarged and congested. In chronic cases the disease is liable to cause cicatricial contraction, with deformity, diverticula formation, and obstruction of part or of the entire seminal vesicle.

When inflammatory or normal contents of the organ are retained, inspissation, calcification, and calculus formation are observed. The calculi are usually very small and contain spermatozoa. They are called by some *symplexion*. Obstruction of the outlet of a seminal vesicle, either from inflammatory or other cause, or of the retention of semen in diverticula of the seminal vesicle, may lead to the formation of cysts known as *hydroceles of the seminal vesicles*.

Tuberculosis of the seminal vesicle is frequent and may be primary or secondary to pulmonary or urogenital tuberculosis. The bacilli may reach the seminal vesicles in the blood, in the lymph, through the vas deferens from tuberculosis of the testis or epididymis, or through the urethra and ejaculatory duct from tuberculosis of the kidneys, bladder, prostate, etc.

The tuberculous vesiculæ seminalis have caseous masses in their walls and the lumen filled with a cheesy exudate.

Tumors of the seminal vesicles are usually secondary to carcinoma of the prostate and rectum, and occur by direct or lymphatic extension.

Primary carcinoma of the seminal vesicles sometimes occurs.

The **spermatic cord,** which consists of the spermatic duct, vessels, areolar tissue, and peritoneum (*tunica vaginalis communis*), is occasionally the seat of varicose veins (*varicocele*), is sometimes inflamed secondarily to surrounding tissues, may become infected with tuberculosis when tuberculous affections are in progress in neighboring tissues, and is occasionally the seat of such tumors as fibroma, lipoma, myxoma, sarcoma, and secondary carcinoma.

The **vas deferens** is frequently inflamed—*deferentitis*. Inflammation is, however, probably always dependent upon infection from the urethra or the testis. It is usually catarrhal and chronic. It may cause infection of the testis and obliteration of its own lumen by the formation of ulcers followed by cicatrization.

Tuberculosis of the vas deferens occurs in consequence of infection from the diseased testis or seminal vesicles; rarely from other sources. It is characterized by the formation of tubercles and tuberculous granulation tissue in the walls of the tube and by necrosis with loss of substance and ulcerations. From the vas deferens infectious material may be carried upward to the seminal vesicles or downward to the epididymis, either of which organs may become secondarily diseased.

Syphilitic lesions of the vas deferens are rare, usually taking the form of fibroid indurations and gummata.

DISEASES OF THE TESTICLE.

Anorchia, or absence of the testicles, is a rare congenital anomaly. It is nearly always associated with accompanying absence of the epididymis, vas deferens, and seminal vesicles of one or both sides. In these cases the individual is apt to retain puerile characteristics, have a small larynx, and no beard or pubic hair.

Monorchia, or absence of one testicle, is more frequent and may occur in otherwise normal persons. Sometimes, although the testicle is absent, the epididymis, the vas deferens, and the seminal vesicle may be present.

Polyorchia, or abnormally numerous testicles, is an almost unknown condition. Probably no well-studied and thoroughly substantiated case is on record.

Microrchia, or hypoplasia of the testicle or of both testicles, is occasionally seen.

Inversio Testiculi.—Sometimes an abnormal position of the testicle is observed, and the free side of the organ is directed backward so that the epididymis is anterior to it.

Cryptorchia, or concealed testicle, depends upon failure of the organ to descend from the abdominal cavity into the scrotum. It may depend upon atrophy of Hunter's bands, adhesions between the testicle and abdominal viscera, obstruction of the inguinal canal by displaced viscera, etc., abnormal and diminutive size of the inguinal canal, especially at the outer ring, and the original abnormal position of the testicle, making its descent impossible. It is a rather frequent condition, and may affect one or both organs.

The testicles may be retained in the abdominal cavity, or, as is more frequently the case, in the inguinal canal. The condition is rather common at birth, showing that the testicle not infrequently descends later in life.

The position of the testicle in the abdominal cavity may make its descent impossible (*aberratio testiculi*), or possible only in an abnormal manner, as toward the perineum, into the internal abdominal ring, and between the muscular layers of the anterior wall of the inguinal canal. The testicles, which do not descend normally, are usually small and incompletely developed, and seem, as a rule, incapable of spermogenesis. They sometimes undergo retrogressive changes, such as fatty metamorphosis, and not infrequently are the starting-point of malignant tumors of a sarcomatous character.

Anemia of the testicle has no importance except when, as the result of arterial obstruction, it may lead to necrosis of the tissues of the organ.

Hyperemia of the testicle is usually an early stage of inflammation of its accompanying vascular phenomenon.

Atrophy of the testis is sometimes observed in marasmus, senility, and chronic inflammatory conditions. The organ is small and dense, having a brownish color, due to pigmentation. The microscopic study shows the epithelial cells of the tubules to be fatty degenerated, and the tubules contain no spermatozoa. Atrophy of the testicle occurs most markedly and earliest in persons affected with arteriosclerosis of the spermatic artery. It also occurs in consequence of the pressure of hernia and in nervous affections, such as paraplegia and certain brain diseases. Inflammatory adhesions may produce pressure atrophy of the testis.

Hypertrophy of the testicle is rare. It is usually compensatory, depending upon loss of function of the opposite organ. Its chief feature is increase in the size of the seminiferous tubules.

Degenerations.—Calcification occurs in the testis in old inflammatory areas and in chronic tuberculosis.

Fatty metamorphosis frequently occurs in the epithelial cells of the tubules in inflammatory, tuberculous, neoplastic, and atrophic conditions.

Colloid metamorphosis is observed in certain of the tissues.

Mucous metamorphosis is also seen in tumors of the testis.

Inflammation of the Testicle—Orchitis—and of the Epididymis—Epididymitis.—Inflammation may affect the testis alone, or the testis and the epididymis, or it may affect the epididymis only. Sometimes the surrounding tunica albuginea is inflamed—*periorchitis*.

Etiology.—Inflammation of the testicle may be acute or chronic. It is usually caused by traumatism and infection, the latter most commonly from extension of the inflammation from the urethra in gonorrhea, prostatitis, or cystitis of infectious nature. In more rare cases the specific cause of the inflammation enters the testicle with the circulating blood, as in pyemia, variola, typhoid fever, mumps, etc. The hematogenous inflammations most frequently occur in the testicle itself, while those resulting from urethral extension and from traumatism are more common in the epididymis.

Orchitis is characterized by hyperemia, inflammatory edema, and swelling of the intertubular tissue of the testicle, causing the organ to become enlarged, sometimes to the size of a goose-egg. It is very firm in texture, and is surrounded by a very tense capsule. If the coverings of the organ be involved, a collection of serous fluid is found in the tunica vaginalis testis —*acute hydrocele*. According to the character of the inflammation, a larger or smaller number of small round-cells will be found both in the intertubular tissue and in the interepithelial tissue of the tubules, and also in their lumen. In traumatic inflammation blood may escape from injured vessels and mingle with the exudate. If the inflammation of the organ be of a mild grade, the epithelial cells of the tubules may show a mild cloudy swelling and cease to form spermatozoa, but if it be severe, the cells will degenerate and desquamate.

The mild inflammations readily recover by absorption of the exudate and regeneration of the lost epithelial elements.

Inflammation of the epididymis resembles inflammation of the testicle.

Purulent orchitis is not frequent. The abscesses may be miliary, or as large as chestnuts. They may be absorbed when small, or may be encapsulated and undergo calcareous infiltration when larger. External rupture is sometimes followed by a marked regenerative reaction in the tunica albuginea, causing the formation of a considerable sized mass of exuberant granulations described as *fungus benignus*.

The escape of the pus into the cavity of the tunica vaginalis sometimes causes violent suppurative inflammation, and may even lead to gangrene of the outer tissues of the scrotum. After evacuation the wound heals by granulation and cicatrization.

The pus of the orchitic abscess, of course, contains the specific micro-organisms, among which may be mentioned the gonococcus, streptococcus, staphylococcus, and typhoid bacillus.

Chronic orchitis not frequently follows the acute form of the disease, and is characterized by a proliferation and thickening of the framework of the organ, by which the connective-tissue hyperplasia becomes more and more marked, and the albuginea and intertubular tissue more and more prominent until the tubular tissue undergoes atrophy. As the disease advances the organ becomes more and more firm and dense, is somewhat reduced in size, and may present an irregular surface. Microscopic examination shows marked increase in the interstitial tissue and diminution in the number of tubules. The remaining tubules are reduced in size and lined with atrophic cells obviously incapable of spermogenesis and more or less advanced in fatty degeneration. In the lumen occasional leukocytes, compound granule cells, and fatty molecules are observed. In the newly formed connective tissue there are many small round-cells as long as there is any inflammation, but after the inflammation is allayed, the tissue becomes dense, tendinous, and cicatricial.

Periorchitis usually accompanies chronic orchitis, and may cause the obliteration of the layers of the tunica vaginalis testis by inflammatory adhesions.

Congenital syphilis not infrequently is a cause of cirrhosis of the testicle.

Epididymitis following gonorrhea or other infections through the vas deferens is sometimes succeeded by chronic inflammation and cirrhosis, with subsequent atrophy. In most cases the inflammation affects both epididymis and testicle simultaneously, and the cirrhotic and atrophic processes occur together in both parts of the organ.

Tuberculosis of the testicle usually begins in the epididymis and affects the testicle proper by lymphatic extension and continuity of tissue. Occasionally it is primary in the testicle itself.

The infection may take place through the circulation or through the vas deferens from the urethra.

I. **Hematogenous infection** may be—

1. *Primary*, that is, a tubercle bacillus accidentally introduced into the circulation may lodge either in the capillary vessels of the testicle or in the epididymis, and produce tuberculosis of the organ. In such cases the tuberculous lesion consists of a primary node which increases in size slowly and usually appears caseous from the beginning. It is usually more or less well encapsulated by connective tissue, but may be surrounded by a zone of granulation tissue containing many fresh gray miliary tubercles, which, as they degenerate, contribute to the increase in size of the original mass. More rarely lymphogenic distribution of tubercles begins early, and numerous tuberculous centers occur.

When the epididymis is first diseased, a mild atrophy takes place in the testicle, followed sooner or later by the development of lymphogenic tubercles, especially in the neighborhood of the rete testis. The tubules of the testicle are separated by proliferated connective tissue which becomes more and more marked as the tuberculous masses are approached. In the tubules are masses of proliferated desquamated epithelium, leukocytes, and occasionally, among these, may be seen giant-cells. Tubular distribution of the tubercles is almost always present.

The primary caseous tuberculous lesion may gradually include all the testicle and epididymis, and form a general caseous mass as large as a hen's egg. Adhesion of the coverings of the testicle usually occurs, and it is not at all uncommon for external fistulous openings to form and permit the escape of caseous material, so that cavities form in the organ. Exuberant granulations may grow from the tunica albuginea and form rather large, spongy, reddish masses about the opening—*fungus testis tuberculosis*.

Primary tuberculosis of the testicle may cause lymphogenic tuberculosis of higher parts of the genito-urinary apparatus, and not infrequently is a cause of general miliary tuberculosis.

2. *Secondary* hematogenous tuberculosis of the testicle is common in most advanced cases of pulmonary tuberculosis, the disease taking the form of small miliary tubercles of interstitial formation. As these increase in size, tubules may be invaded and may afford an avenue of escape for the cheesy tissue.

In both the primary and secondary form of testicular tuberculosis tubercle bacilli may be excreted with the spermatic fluid, which becomes infectious.

II. **Urethral infection** takes place when tubercle bacilli, entering the urine from other varieties of urogenital tuberculosis, accidentally find their way into the vas deferens. In a few reported cases in which tuberculosis of the testicle seemed to follow gonorrhea with orchitis or epididymitis the disease was probably already present and only accelerated in development by the added infection. The urethral infection occurring through the vas deferens is primarily tubular, and more likely to begin in the epididymis than in the testis proper. It is rare compared to the hematogenous form of infection.

Syphilis of the testis and epididymis occurs in both congenital and acquired syphilis. The chief lesions are *intertubular round-cell infiltration*, associated with tubular atrophy and induration. The large cellular infiltrations sometimes undergo caseation, with the formation of *gummata*, which are usually small and multiple, but may be large. Evacuation may be succeeded by the formation of fungous syphilitic granulations. The testicle is more frequently affected than the epididymis.

Cicatrization following gumma formation and succeeding the round-cell infiltration is very dense, often predisposing to further atrophy of the affected organ.

Lepra sometimes causes nodular formation in the testis, followed by degeneration and atrophy.

Cysts of the Testicle.—Spermatocele.—The cyst known as spermatocele usually develops at the head of the epididymis, and less frequently at its tail. It forms a large, smooth-walled cyst, the contents of which may amount to 350 c.c. The fluid is watery, slightly turbid, and when examined microscopically, is found to contain spermatozoa, which may be actively motile, non-motile, or degenerated, according to the length of time they have been present. It is probable that in the course of time the spermatozoa entirely disappear and leave a clear fluid. The spermatocele is probably formed by the accumulation of fluid in the lower blind end of the Wolffian body, into which the spermatic fluid enters by regurgitation from the common duct. The wall of the cyst is lined with cuboidal epithelium.

Serous cysts, attached by long pedicles to the head of the epididymis, occur in consequence of dilatation of the blind end of retained Müller's ducts.

Retention cysts of the testicle depend upon obstruction of the vasa deferentia and tubules. Tubules of the epididymis, more frequently than those of the testis, show the dilatation, especially in the neighborhood of the head of the epididymis. The majority of these cysts are small. The contents may be milky (*galactocele*), or may be clearer and contain spermatozoa. The walls of the cysts are smooth and lined by columnar or cuboidal epithelium. Usually the cysts appear to be superficial, but they may be deeply seated.

Retention cysts also occur in combination with neoplastic developments in the testis, associated with obstruction.

Dermoid cysts are much less frequent in the testis than in the ovary. The tumor is usually seated in the substance of the organ, sometimes surrounded by a connective-tissue capsule containing fatty tissue. (See Dermoid Tumors.)

Parasitic Cysts.—Echinococcus cysts have been observed in the testis and also in the epididymis.

Tumors of the Testicle.—**Fibroma** usually develops from the tunica albuginea, and sometimes from the wall of the vas deferens. The tumors have the usual macroscopic and microscopic appearances, and are prone to calcification.

Lipoma is a rare tumor developing from the covering membranes of the organ, and sometimes from the tissue of the vas deferens.

Myxoma is a rare tumor of the testis. Myxomatous degenerations and the formation of mucous tissue in combination with other tumors are common.

Rhabdomyoma is occasionally observed in the testis. The growth seems to spring from the tunica albuginea, and consists of a fleshy mass of striped-muscle cells which may entirely replace the testis or occupy only a part of its substance.

Chondroma.—Pure cartilaginous tumors of the testis are rare. They may form rounded, single nodules of various size, or may be multiple and of various size. I have seen one that extended throughout the substance of the testis in a dendritic form. The tumor is somewhat malignant in tendency, and growing in the lymphatic spaces and vessels, gives metastasis to the inguinal glands and later to the lungs. Secondary fibrous, cystic, and atrophic changes occur in the testicle as a result of the growth of this tumor. The primary growth usually occurs in the rete testis.

Combinations of cartilage with various other tumor tissues are much more frequent than pure chondroma—thus, chondrosarcoma, chondroadenoma, and chondrocarcinoma are not infrequent mixed tumors.

Osteoma of the testis has been seen by Neumann. The tumor formed an irregular mass, more or less nodular on the surface, which occupied the left testis. Its structure was true spongy bone with fatty marrow. In fibrous areas or islands in the bone small masses of hyaline cartilage not connected with the bone were observed.

Sarcoma.—Sarcomata of all varieties occur in the testicle, and rather less frequently in the epididymis. Round-cell, spindle-cell, giant-cell, and alveolar sarcomata, angiosarcomata, and pigmented sarcomata are all occasionally met, sometimes in the pure form, but much more frequently in mixed, one part of the tumor being a simple cellular growth, another part alveolar, still another part telangiectatic, etc. Sarcoma of the testicle is also prone to combine with the higher tissues, so that fibrosarcoma, myxosarcoma, lipomasarcoma, etc., are frequent. Degenerations are also frequent, and cysts are formed by softening. Cysts are also formed by dilatation of the seminiferous tubules, so that *cystosarcoma* of the testis may have a double meaning.

One of the most interesting of the tumors of this class somewhat resembles the intracanalicular tumors of the mamma, in that ingrowths of the tumor tissue take place into the cysts, with the production of more or less marked polypoid excrescences almost filling up the original cysts.

Cysts.—Cysts of the testis that form through metamorphosis of tumor tissue are irregular cavities with indefinite walls, and are filled with the products of tissue destruction. The retention cysts are smooth-walled, lined with columnar and cuboidal epithelium, and contain either a clear fluid or a semicaseous mass composed of fatty degenerated epithelium, fat-drops, and cholesterin plates. Cysts of this kind are sometimes described as *cholesteatoma testis.*

The mixed tumors of the testis are probably all congenital teratomata.

Perithelioma of the testicle has been observed by Waldeyer.

Endothelioma in the testis is not infrequent, but is easily confused with carcinoma and adenoma.

Adenoma of the testis is rare; most of the growths resembling adenoma are cystic (*adenocystoma* and *adenocystoma papilliferum*) and may show irregular epithelial outgrowths in all directions—*adenocarcinoma*.

Tumors of this kind are usually observed in middle life. They most frequently affect the testis, leaving the epididymis unchanged. The contents of the cysts vary, some being mucous, others mushy, so that *mucous* and *atheromatous* cystadenomata have been described.

Carcinoma of the testicle is not uncommon. It may be a simple and easily recognized tumor, encephaloid or scirrhous in nature, or may be complicated by admixtures of various of the simple tissues. The encephaloid tumors are most frequent.

The neoplasm develops from the glandular cells of the seminiferous tubules. The growth of the tumor usually takes place from some single focus, but the non-carcinomatous portions of the organ show catarrhal and retrogressive changes. In the course of time the entire organ becomes transformed into carcinoma. The tumor itself is prone to interstitial hemorrhage and to mucous degeneration.

Macroscopically, the growth varies in size, is irregular in form, soft or hard according to the amount of interstitial tissue present, and upon section appears variegated, the cellular parts contrasting with the fibrous tissue and interstitial hemorrhages and degenerations.

In the epithelial masses it is not infrequent to observe colloid degeneration and the formation of cysts—*cystocarcinoma* or *colloid carcinoma*.

Carcinoma of the testis usually develops from the testis itself, but subsequently invades the epididymis and vas deferens. In cases in which the very resisting tunica albuginea is perforated the disease usually rapidly infiltrates the skin of the scrotum.

DISEASES OF THE TUNICA VAGINALIS TESTIS.

Vaginitis testis, also called **periorchitis** and **vaginalitis,** is a common affection. It may follow inflammation of the testicle or epididymis, specific infectious diseases, as scarlatina, typhoid fever, mumps, etc., may depend upon traumatism, and sometimes occurs from causes not discoverable. The disease is apparently more frequent in southern than in northern latitudes, and is most common during middle life.

The vaginal inflammations may be acute (in traumatic injuries and gonorrheal infection) or chronic, and may be serofibrinous, purulent, hemorrhagic, adhesive, and villous.

The serofibrinous form of vaginitis testis is characterized by an accumulation of fluid in the tunica vaginalis testis, and the condition is known as *hydrocele vaginalis*. It probably depends chiefly upon inflammatory reaction, though its frequent chronicity suggests that from some cause the equilibrium of exudation and absorption of fluid in the cavity of the tunica vaginalis has been destroyed. Rapidly or slowly, in different cases, fluid collects in the tunica vaginalis, until in some cases it becomes greatly distended. A pint of fluid is very commonly seen, a quart is by no means rare, and at least one case is recorded in which 3000 cubic centimeters were present. The condition is, as a rule, unilateral. If the vaginal process of peritoneum remains open so that the cavity of the tunica vaginalis and abdomen remain in communication, the contents of the hydrocele can be driven up into the abdominal cavity. This condition is called *hydrocele peritoneovaginalis*. *Bilocular* and *multilocular hydroceles* are the result of division of the sac by preëxisting or newly formed bands of any kind.

In the beginning the fluid is found to be somewhat turbid from the presence of minute fibrin flakes and leukocytes, but later it becomes clear and much resembles freshly voided normal urine. It is albuminous, and, like the fluids from the chest and abdominal cavities, sometimes coagulates spontaneously.

The fluid of a hydrocele is sometimes milky in appearance and contains cholesterin plates. It may become considerably inspissated and mushy, and in some cases is pigmented. Macroscopically the hydrocele forms a pear-shaped enlargement of the scrotum, the apex being directed toward the inguinal ring. The fluid ascends as high as the patulous funicular process permits.

In rare cases the microscopic study of the fluid reveals the presence of some spermatozoa that probably owe their presence to the preëxistence of a spermatocele that has emptied its contents into the hydrocele; or, as Roth has explained, from seminal fluid emptied into the cavity of the tunica vaginalis from an open *vas aberrans* from the head or the base of the epididymis, or from the free end of Morgagni's hydatid. In the latter case the condition is a congenital anomaly. Hydroceles in the fluid of which spermatozoa are found are called *hydrocele spermatica*.

The secondary results of hydrocele are observed in the membrane, which eventually becomes much thickened and indurated, although it is usually not altered in the beginning, and in the testicle and epididymis, which are indurated and sometimes atrophic. These latter changes are more probably incited by the inflammation than by the pressure exerted by the fluid.

Ununited spaces in the closed funicular portion of the vaginal process sometimes begin to accumulate serous fluid late in life and form hydrocele-like dilatations known as *hydrocele funiculi spermatici cystici* or *hydrocele extravaginalis*. They may occur as complications of simple hydrocele.

Hydroceles are sometimes *congenital*, and depend upon communication of the vaginal process and peritoneal cavity, by which the peritoneal fluid sinks down into the scrotum and causes dilatation. In most of these cases, however, the etiology is not so simple, for inflammation is observed in the tunica vaginalis and no doubt the process is partly inflammatory.

Hemorrhages into the tunica vaginalis testis occurring from traumatic injuries, hemorrhagic diatheses, etc., lead to the formation of hematocele. The blood may remain unaltered for a long time, but finally dissolves, liberates pigment, and is transformed into a clear fluid. Fibroid indurations usually follow.

Lymphorrhagia, with the formation of *galactocele*, is sometimes observed in tropic countries and is probably of parasitic origin (*filariasis*).

Vaginitis Purulenta or Suppurative Periorchitis.—Suppuration of the tunica vaginalis testis most frequently succeeds traumatic injuries of the scrotum, rupture of abscesses of the testicle or epididymis, or of superficial parts into the tunica vaginalis testis, hematogenous infection, or infection of preëxisting hydrocele, the most usual cause of the latter accident being operation for the relief of the affection.

The condition is characterized by a purulent accumulation in the tunica vaginalis testis, with fibrinopurulent exudation upon the serous surface and maceration of the tissues. In cases of infection with putrefactive organisms, in addition to the suppuration one may observe fetor and sometimes gangrene of the inflamed parts.

Loculated purulent accumulations or sacs of pus resulting from inflammation of local open areas of the vaginal process are sometimes spoken of as *purulent perispermatitis*. The affection may terminate by absorption of the exudate, by external evacuation of the pus, or by granulation accompanying absorption, by which firm fibrous union between the layers of the membrane is accomplished.

Vaginitis Hæmorrhagica.—Traumatic injuries of the scrotum are often followed by hemorrhagic exudations into the tunica vaginalis testis, which serve to complicate the process of healing. They may appear as distinct blood collections (*hematocele*) or as punctiform or larger subserous infiltrations.

In the process of organization in the plastic or productive vaginalitis the newly formed blood vessels often allow considerable leakage from their delicate, unsupported walls, thus causing blood to be added to the exudate. This addition seems to embarrass the processes of repair, and not only do firmer fibrous unions occur in these cases, but considerable-sized accumulations sometimes as large as the first occur (*hematocele*), undergo solution, and form clear fluid collections with pigmented walls. The greatly thickened scrotal walls not infrequently calcify or even ossify. The testicle atrophies.

Plastic Vaginalitis.—The various forms of vaginalitis are commonly followed by fibrous union between the layers of the serous membrane. The adhesions form in the same manner as those of the pericardium and peritoneum. The sac may be completely obliterated, or may be divided by partition into numerous small sacs, which, when they subsequently become the seat of exudative inflammation, form multilocular cysts. According to the variety, severity, and duration of the vaginitis the adhesions will be delicate or coarse.

Villous Vaginalitis.—Villous or verrucose vaginalitis is a form of plastic vaginitis testis in which sessile or pedunculated excrescences develop from the serous covering of the epididymis. They sometimes occur in other parts of the membrane. They are probably hypertrophies of the villosities, and are so frequently observed in the covering of the epididymis as to be regarded by Luschka as normal. At other times they may be formed of granulation tissue.

Tuberculosis of the tunica vaginalis is usually secondary to tuberculosis of the testis or epididymis. It presents the form of disseminated tubercles with cloudy fluid in the cavity.

Syphilis may bring about fibroid induration of the serous membranes. Gummata are occasionally seen, but usually the changes follow disease of the testis. Hydrocele is sometimes of syphilitic origin.

Tumors are rare in the tunics of the testis. Fibroma, myxoma, sarcoma, and rhabdomyoma have been described. Dermoid cysts are sometimes found.

Parasites.—The Tænia echinococcus has been observed once in the vaginal membrane.

DISEASES OF THE FEMALE SEXUAL ORGANS.

THE OVARIES.

Congenital malformations of the ovary are unusual. Total absence of both ovaries in otherwise well-formed individuals probably does not occur. Unilateral absence of ovaries is occasionally seen, especially in uterus unicornis. Rudimentary development of the ovary occurs, together with imperfect development of other of the sexual organs, in dwarfs, in cretins, and in chlorosis. Abnormally large ovaries depending upon excessive growth of the follicles are not infrequent.

Sometimes the ovaries are divided by the detachment of small lobes, or supernumerary ovaries may be present. In infancy the ovaries are relatively large and lobulated; in senility small, deeply scarred, and cirrhotic.

Not infrequently the ovary descends like the testicle and may be found in the inguinal canal (*hernia of the ovary*) or in a labium majus.

The ovaries vary in size and appearance according to the age and sexual development of the individual. In infancy they are small, pinkish in color, and more or less lobulated; at puberty they begin to grow and attain their maximum development about the twentieth year. During the sexual life of the individual they maintain an average size, diminishing again by atrophy and induration until, in the very aged, they become small, deeply scarred, dense white bodies.

Hyperemia of the ovary is a common pathologic and physiologic condition. During the period of sexual activity the ovary is richer in blood than before or after. At the periods of menstruation the ovaries enlarge and become soft and congested. The rupture of follicles and escape of ovules are always followed by hyperemia. All forms of inflammation of the uterus and tubes are liable to be associated during the acute stage with congestion of the ovary. Puerperal infections are commonly associated with it. The ovary, when hyperemic, appears enlarged, reddish in color, soft, and elastic.

Passive hyperemia of the ovary is observed in obstructive heart disease. The ovaries appear dark purple in color.

Hemorrhages of the ovary occur at the time of the rupture of the follicles. The blood escapes into the follicle, infiltrates the substance of the ovary more or less, and perhaps occasionally escapes into the abdominal cavity, to collect and coagulate in the pelvis and cause adhesions. Hemorrhages also occur in the hemorrhagic diatheses, such as scurvy, and in the infections and intoxications. Interstitial and follicular hemorrhages may form *hematomata*.

Oöphoritis, or **inflammation of the ovary**, may originate by the hematogenous distribution of bacteria, but is most frequently caused by infectious agents (streptococci, staphylococci, gonococci, etc.), which ascend to the ovary from the uterus and tubes. Puerperal infection is the cause in nearly all cases. It may also occur in consequence of lymphogenic extension of inflammations from neighboring organs, as perimetritis, peritonitis, etc.

The early stages of the inflammation are characterized by hyperemia and inflammatory edema of the organ, which becomes much enlarged, soft, juicy, and contains numerous hemorrhagic infiltrations. Round-cell infiltrations are very common in the interstices of the tissue, and occasionally form small abscesses. In rare instances fair-sized abscesses may occur. The follicles are particularly affected, and when suppuration forms, the chief feature of the process, the purulent collections correspond to follicular dilatation and destruction. In rare cases an entire ovary may be transformed into a sac of pus surrounded by a thick but easily lacerable encasement of edematous fibrous tissue.

Oöphoritis usually terminates by absorption, the purulent as well as the serous and hemorrhagic contents being thus taken up after the acme of the inflammation has passed. Small abscesses usually become surrounded by fibroconnective-tissue encapsulations and may be found long afterward.

Rarely the abscesses rupture into the abdominal cavity, producing peritonitis. If, however, the gonococci, streptococci, or other pyogenic organisms in the pus have died, the pus is sterile and rupture of the abscesses is without ill effect. In rare cases the inflammation of the ovary is fatal through general septic infection.

Inflammations of the ovary may be described as *oöphoritis serosa*, *oöphoritis hæmorrhagica*, *oöphoritis necrotica*, and *oöphoritis purulenta*, according to the appearances presented.

Acute oöphoritis is sometimes caused in the infectious diseases, such as typhoid fever, cholera, etc., by hematogenous germ-distribution, but depends chiefly upon puerperal infection through the genital organs. Rare cases of necrotic oöphoritis are said to have resulted from arsenic, phosphorus, and other poisonings. Acute oöphoritis sometimes terminates in a chronic condition characterized by cicatricial tissue formation and contraction.

Chronic oöphoritis is characterized by the formation of fibroconnective tissue and by contraction. It leads to induration, cicatrization, and contraction of the ovary. It must be remembered, however, that the changes characteristic of the affection are all in a certain sense normal to the ovary, and that from the time it reaches sexual maturity until death there is an uninterrupted series of follicular enlargements, ruptures, and proliferations by which the ovary ultimately becomes transformed into a diminutive, dense, fibrous, scarred organ, the normal stroma of which is almost entirely transformed into connective tissue and no longer contains ovules.

Peri-oöphoritis is of frequent occurrence from disturbances occurring within the ovary itself, as well as from inflammation of the surrounding structures. The capsule of the organ seems to lose its epithelial covering and to become thickened, indurated, and deeply scarred where follicular ruptures have taken place. Fibrin sometimes exudes upon the surface, gluing the organ to surrounding tissues, to which it may adhere strongly by newly formed fibrous bands. The contraction of the capsule reduces the size of the ovary, and the density of its structure prevents the rupture of follicles which necessarily dilate and form cysts.

Follicular cysts of the ovary result from an abnormal development of the Graafian follicles, which, when ripe, instead of rupturing and discharging the contained ovules, continue to enlarge after the death of the ovule itself. The cause of the enlargement, which may affect one or many follicles, is supposed to be an abnormal resistance of the capsule,—tunica albuginea,—probably depending upon previous peri-oöphoritis. The condition is seen chiefly during the period of sexual activity, and, as a rule, a number of follicles are enlarged at the same time. The contents are usually fluid, clear, and limpid in character, but may be mixed with blood. As the cysts enlarge, the mutual pressure not infrequently causes the intermediate tissue to atrophy, so that single large cysts may form from several small ones. Single large cysts also form from the dilatation of single follicles. As the cysts enlarge the ovarian tissue is attenuated more and more until the tension and pressure cause its ovules and unripe follicles to disappear, transforming it into a mere appendage. The cysts usually show an epithelial lining and occasionally may contain numbers of ovules.

The cysts may become as large as a man's fist, or even as large as a child's head. When the walls are very thin, rupture and discharge of the contents into the abdominal cavity may occur, this accident usually being harmless. Rupture may also occur into a Fallopian tube, producing a *tubo-ovarian cyst.* When the lower end of the tube is unaltered by disease, tubo-ovarian cysts may periodically evacuate through the uterus.

Cysts of the parovarium occur from increased exudation into its tubules, which latter, in consequence, becomes much dilated. These cysts are situated in the broad ligament, and the fluid contained within them is clear and limpid.

Tumors of the Ovary.—Tumors of the ovary are peculiar in that the great majority of them are cystic. Of 1388 ovarian tumors studied by Olshausen, only 137 were solid. Solid tumors are usually small and benign; many of them are discovered only at autopsy, so that the great majority of the ovarian tumors that present themselves clinically are cystic. The difference between the simple follicular cysts already described and the cystic tumors is that the former occur in the ovarian tissue and the latter in the morbid growths. These cysts may develop concomitantly with the tumor as essential elements of its structure, or be subsequently formed within it by colliquation. Probably the majority of the ovarian cysts are of the former class, and are properly placed among the *cystic adenomata.* The solid portions of the tumors consist of embryonal or sometimes well-formed connective tissue, which may closely resemble spindle-cell sarcoma if the tumors be of rapid development. The elements from which the cysts are formed, according to the accepted etiology, take their origin from the *Pflüger's tubes* of the embryo.

When examined critically, the tumors can be divided into two groups: simple cystoma and papilliferous cystoma (*q. v.*).

Aside from the difference in the origni of these cysts and the fact that they occur in a neoplastic stroma, there is a histologic difference that separates them from the follicular cysts. They are not mere dilated follicles, but each is surrounded by a dense fibrous tissue, upon which is a vascular membrana propria supporting the glandular elements. The epithelium is usually columnar in type, and in rare instances is ciliated. As the tumor continues to grow new glandular tubules are constantly formed in the walls of the already existing cysts, and in their turn become cystic; hence nearly all the tumors are *multilocular.* As the cysts increase in size, atrophy of the walls causes them to unite and remnants of the former septa often hang like papillary outgrowths or long villi from the cyst-walls. This should be remembered lest an erroneous diagnosis of papilliferous cyst be made.

The tumors vary in size, sometimes weighing over 100 pounds. They are commonly as large as a cocoanut, and are, as a rule, rounded growths, smooth on the surface, and attached to the body by a pedicle of small size, which represents the ovarian ligament, or in some cases the broad ligament with the ovarian vessels. Adhesions may form between the tumor and surrounding organs.

The cysts contain clear limpid fluid or dense colloid jelly. As a rule, the contents are adhesive and gelatinous. They may be colorless or yellowish or bluish-white in color. Eichwald finds the chief ingredients to be albumin-peptone, paralbumin, and metalbumin. The small cysts contain colloid, mucin, and mucipeptone. Paralbumin is found by Hammarsten to be a mixture of albumins, chiefly serum-albumin, with metalbumin, which, because of its relationship to mucin, he calls *pseudomucin.* Pseudomucin differs from mucin in that it is not acted upon by acetic acid, while mucin is precipitated.

The **papilliferous cystoma** is a multilocular cyst from the walls of which papillary outgrowths of various size occur. Marchand restricts the definition so as to make it apply only to tumors whose papillary processes carry ciliated epithelium. There may be but few of the papillæ, and they may be of small size, but usually they are numerous and dendritic, and may completely fill the cysts. This papillary formation may make it easy to mistake the cystic for solid tumors. Both cyst-walls and papillary projections are covered with columnar epithelium in which goblet cells are sometimes numerous. The contents of the cysts resemble in other particulars that of the simple cystoma, and, like them, are produced by the cells. Pseudomucin is said to occur less frequently in papilliferous cysts than in simple cysts.

The **simple cystoma** is a benign tumor, though the papillary cystoma with marked activity of growth is likely to be malignant and occasion abdominal metastases. The more active the growth of the tumor and the greater the rapidity of the growth of its cells, the more malignant its tendency. Indeed, in some cases the cells develop so rapidly as to fill up the surrounding space and produce a condition histologically resembling carcinoma. Ziegler applies the name *cystoma papilliferum carcinomatosum* to tumors of this kind. The rapid growth of the epithelium causes it to outgrow the confines of the cyst and to rupture its surrounding walls, after which it sometimes develops as a cauliflower-like mass upon the surface of the tumor.

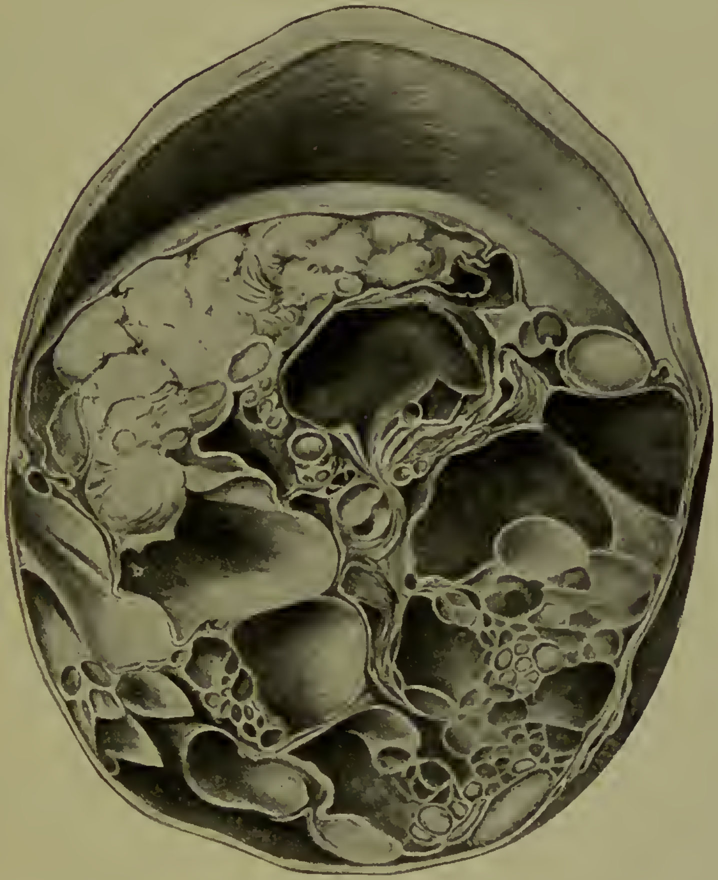

FIG. 312.—Cystoma of the ovary. The organ is divided by a longitudinal section, one half being shown in the illustration. Many of the cysts are distinctly shown, some of them being filled with colloid material.

Rarely, concentric calcareous bodies occur in the walls of the papilliferous cysts and sometimes in the papillæ. They consist chiefly of carbonate of lime.

It is not known whether the histogenesis of the papillary tumor with ciliated epithelium is identical with that of the simple cystoma or not.

A curious modification of the papilliferous tumor is that seen affecting sometimes one but usually both ovaries, in which, instead of the papillary growths developing in cysts in the body of the tumor, they are chiefly superficial or even entirely superficial, the tumor itself being solid. Just how this modification occurs or from what histologic elements it takes its development is not clear. That the tumor is identical with the cystic form seems evident from the fact that it is of villous character, that the epithelial cells are frequently ciliated, that the stroma and villi frequently contain the concentric calcareous bodies, and that the tumor is likely to undergo the carcinomatous development already described and give metastasis to the abdominal organs.

Dermoid cysts are more frequent in the ovary than in any other organ. (See Dermoid Cysts.)

Carcinoma of the Ovary.—Carcinoma of the ovary may develop independently of any preëxisting tumor. In such cases it is supposed to have its histogenesis directly in the cells of Pflüger's tubes or in the follicles. It is peculiar in that it occurs at any age and is frequent in youth and childhood. It causes the ovary to become transformed into an enlarged nodular mass from which the follicles speedily disappear. When examined microscopically, it presents the usual histologic appearances. The tumor may affect both ovaries simultaneously and symmetrically. It may be dense and firm—*scirrhus*—or soft and cellular—*encephaloid*. Not infrequently myxomatous degeneration occurs in the carcinoma cells; sometimes in the stroma. The tumor is metastatic.

Colloid carcinoma of the ovary sometimes occurs.

Wilms and others have seen *squamous epithelioma* develop from dermoid cysts of the ovary.

Carcinoma of the ovary is malignant, gives rapid metastases to the abdominal organs, and causes death in a short time.

Secondary carcinoma of the ovary is almost unknown. When neighboring viscera are the seat of carcinoma, the ovary is rarely invaded. This, no doubt, indicates an independent lymphatic supply.

Fibroma sometimes occurs in the ovary. It may be single or multiple. Its origin is referred by some to overgrowth of the corpora fibrosa.

Large *fibrosarcomata* involving the entire ovary occasionally occur. These tumors usually correspond in shape to the ovary, but are large and sometimes nodular. There are sometimes gland-like elements present in the fibrous tissue—*adenofibroma*.

Chondroma does not occur independently of teratoid combinations.

Fibromyoma has been described, but probably occurs only as a teratoid combination.

Sarcoma is a rare primary tumor of the ovary. Both the round-cell and spindle-cell forms occur, *angiosarcoma* being most frequent. The tumor is likely to undergo myxomatous degeneration. It is usually mildly malignant in disposition, and not prone to give wide-spread metastasis. Sarcoma in the ovary is quite likely to be bilateral and may be congenital. Doran saw bilateral sarcoma of the ovary in a three-months' fetus.

Large round-cell sarcoma is more frequent than the small round-cell form. Combinations of round-cell and spindle-cell forms are by no means rare. Epithelial glandular tissue is occasionally found in sarcomata—*adenosarcoma*.

The tumors may become very large. They usually form smooth, rounded, more or less indented or nodular tumors, without a disposition to infiltration. Metastasis is sometimes rapid, but is often delayed.

The sarcoma tissue usually invades the ovary, separating and disorganizing its tissue so that the follicles and ovules before their destruction may seem to lie in the tumor tissue. *Colliquation cysts* are frequent in these tumors.

Endothelioma sometimes occurs.

Cavernous angioma is very rare in the ovary.

Parasites of the ovary are rare. Echinococcus cysts have been observed.

DISEASES OF THE FALLOPIAN TUBES.

Congenital malformations of the Fallopian tubes are usually associated with malformations of the uterus. During the period between the eighth and twelfth weeks of embryonal life the lower portions of Müller's ducts coalesce, and form a single tube, of which the lower part becomes the vagina, the upper part, the uterus. In the fourth or fifth month the uterus begins to grow out on the sides, forming the horns with which the Fallopian tubes connect. These horns later become incorporated with the body of the organ. Malformations of the tubes depend chiefly upon malformations of the uterus. Thus, if one horn of the divided uterus of the fifth month should alone develop, the other horn remaining rudimentary, its Fallopian tube might be either perfectly formed or also hypoplastic, or even reduced to a simple fibrous cord. Absence of the tubes is rare except in cases of very defective development of the sexual organs. In rare cases the tubes are separated from the uterus and open at both ends into the abdominal cavity. The tubes may in rare cases be simple fibrous cords; in other cases they may be atresic at the lower end, or in rarer cases, constricted or closed at the middle part.

Hyperemia of the tubes occurs with the advent of menstruation, at the time of follicular rupture, and perhaps during coitus. Slight *hemorrhage* may result from the congestion, and the blood may pass from the tubes into the abdominal cavity.

The tubes are usually symmetrically affected because of the relation they bear to the uterus. In physiologic conditions the nervous impulses affect both tubes simultaneously. In the infectious diseases caused by the entrance of micro-organisms from the uterus, the infectious agents enter both tubes. Exceptions are occasionally seen.

Salpingitis, or inflammation of the Fallopian tube, is probably always infectious, and results from the entrance of micro-organisms into the uterine end of the tube. It follows endometritis, especially puerperal endometritis, and gonorrhea. Infection may occur through the fimbriated end in pelvic peritonitis. The micro-organisms associated with salpingitis are those ordinarily associated with suppuration, especially the gonococcus.

A. Martin bacteriologically studied 376 cases and succeeded in demonstrating the gonococcus in 76; streptococci and staphylococci in 50; pneumococci in 7; and Bacterium coli communis in 1.

From numerous bacteriologic examinations it seems to be established that gonococci often, if not usually, die out comparatively early, leaving the accidentally present pyogenic bacteria to carry on the suppuration for a time. Later these also disappear, so that the exudates in cases that have persisted for a long time are usually sterile.

Salpingitis no doubt originates as a catarrhal inflammation of the mucous membrane of the tube, and is accompanied by an exudation which may be mucous, mucopurulent, purulent, or hemorrhagic, according to its severity. Occasionally diphtheritic inflammations are observed. They are usually associated with wide-spread necrosis of the epithelium. The products of inflammation probably at first escape into the uterus, where, if the infection of the tube has been primary and no preliminary endometritis existed, an inflammation of mild severity may occur, or the secretion being too thick to escape readily through the small uterine end of the tube, ascends and escapes upon the fimbriæ, ovary, etc., causing inflammation. This external inflammation has an important bearing upon the subsequent changes, for the peritoneum becomes coated with a fibrinous exudate and adhesions form between the ovary and tube, between the tube and the uterus, and later between the fimbriæ, which are drawn in toward a common center and cemented together, so that in time the upper, funnel-shaped, open, fimbriated extremity of the tube becomes smooth, rounded, and closed. Closure from inflammation, kinks, etc., is followed by retention of the exudate and dilatation of the tube. The tube becomes greatly increased in diameter, elongated, and serpentine. Its surface is usually smooth and may be free from adhesions.

Various names are applied to the condition according to the character of the exudate. Thus to cases associated with considerable hemorrhage into the tubal cavity the name *hematosalpinx* or *hæmatoma tubarum* is applied. Cases with purulent exudate, which are most common, are called *pyosalpinx*, and cases with seromucous exudate or with a watery exudate are called *hydrosalpinx*.

It may be inferred that the larger the serous collection, the older it is. In some cases hydrosalpinx attains the size of a goose-egg; pyosalpinx is usually smaller.

The changes are not all confined to the mucous membrane of the tube. The mucosa and subjacent tissues become greatly edematous, and, in pyosalpinx, much infiltrated with pus. Here and there the lining epithelium is lost, and denuded rugæ have their surfaces brought into contact, so that subsequent union may occur, with the inclusion of larger or smaller spaces lined with epithelium, the secretion of which may cause subsequent dilatation into cysts.

The muscular walls early become edematous, subsequently hypertrophy, and by lymphogenic metastasis often contain numerous small miliary abscesses. When the lesions become old and considerable hydropic distention occurs, the walls yield and become attenuated, transparent, and membranous in character. There is always danger that fluid collections will rupture from softening, from suppuration, or from the accidental pressure of the pelvic and abdominal organs. In the purulent form of the disease such an accident may be fatal from ensuing septic peritonitis; in the stage of hydrops it may be of little importance. The perforation may take place into a pseudomembranous surrounding sac, caused by a previous perisalpingitis; or in more rare instances may occur through the wall of the bladder or rectum, which has been united to the tube by inflammatory adhesions.

Peri-oöphoritis, pelvic peritonitis, and perimetritis may be secondary to salpingitis.

Salpingitis is nearly always bilateral and symmetric, but may be a little more advanced on one side than on the other.

Tuberculosis of the Fallopian tube is a rather rare affection, not occurring oftener than in 2 to 8 per cent. of cases examined by different authors. Williams found tuberculosis in 8 per cent. of the tubes removed for chronic inflammatory conditions at the Johns Hopkins Hospital. The disease occurs both in children and adults, and is usually bilateral, though it may affect one tube only. In the majority of cases it is probably secondary to chronic tuberculosis of the lungs and other organs. Primary tuberculosis of the genital organs is more common in men than in women.

The tuberculous infection may be favored by preëxisting pyosalpinx, for, according to Williams, it is not infrequent for tubercle bacilli and gonococci to occur simultaneously in the tube.

Tuberculosis of the tubes in the form of scattered miliary tubercles may also occur in general miliary tuberculosis, or may succeed peritoneal tuberculosis in the form of minute tubercles scattered over the serous and mucous surfaces, or of more or less circumscribed cheesy infiltrations between the isthmus and ampulla of a tube. The discharge of tuberculous material into the uterus may lead to its secondary infection and establish tuberculous endometritis.

Tuberculosis salpingitis is usually associated with firm adhesions between the tube and ovary, and secondary invasion of the ovary is frequent. Primary tuberculosis of the Fallopian tubes is always of hematogenous origin.

Syphilis of the Fallopian tube is rare and characterized by gummata and diffuse fibrous thickenings, which are said to reduce the tube to a contracted fibrous cord. Syphilis of the tubes has been observed in fetuses and in newborn infants.

Tumors of the Fallopian tube are of infrequent occurrence. *Fibroma*, *myofibroma*, and *fibromyoma* are said to occur, usually from the outer layers of tissue. They are sometimes sessile, sometimes pedunculated, and may be calcified. In the broad ligament of the tube small *lipomata* are occasionally observed. *Papilloma* of the mucous membrane has been observed. *Carcinoma* of the tubes may be primary or secondary, the former originating in small papillary outgrowths of the mucous membrane, the latter in primary carcinoma of the uterus or ovary. *Sarcoma* is rare. It is usually of the spindle-cell variety, though round-cell sarcoma has been observed. Ohlfeld and Marchand have observed *syncytioma malignum* in the tube.

Cysts.—The most frequent cysts are caused by tubular distentions and have already been described as *hydrosalpinx*. Next to these are cystic remnants of Müller's ducts, which, attached by a more or less elongated pedicle, are found connected to the fimbriated extremity, broad ligament, and tubes. They are about the size of a pea or bean. The little cysts are usually called after their describer—*hydatids of Morgagni*. They are present in about 20 per cent. of cases examined.

DISEASES OF THE UTERUS.

Congenital anomalies of the uterus are, for the most part, the result of the irregular fusion of Müller's ducts. These embryonal structures unite between the eighth and twelfth weeks of embryonal life to form a simple canal, the upper part of which becomes the uterus, the lower part, the vagina. If one of Müller's tubes fails to develop and unite with its fellow, or does so imperfectly, the result is a unilateral deformity. If both Müller's ducts develop imperfectly, a rudimentary organ results. If the ducts fail to unite, double uterus and sometimes double vagina may occur. If the ducts unite except at the fundus of the future uterus, an organ with two horns occurs. In this manner are formed:

Uterus infantilis—the result of imperfect development with perfect fusion of Müller's ducts—is characterized by very diminutive size of the uterus and the vagina. The ovaries and tubes rarely attain more than rudimentary development.

Uterus unicornis, or unilateral asymmetry of the uterus, is formed by failure of one of Müller's ducts to attain perfect development. The result is a small uterus with a marked obliquity of position, and having an auxiliary attachment in the form of a fibrous cord or atypical muscular canallated mass at the lateral margin near the fundus, representing the undeveloped Müller's duct. The ovary of the well-developed side is normal and functional, that of the other side, rudimentary. The condition does not interfere with conception and pregnancy, except that the rudimentary attachment may rupture in the middle months of pregnancy.

Uterus bicornis results from failure of Müller's ducts to coalesce properly. It may appear in an unusual prominence of the horns of the uterus and in an unusually marked tendency to division at the fundus, with a suggestion of a partition formed by downward extension of the muscular and endometrial substance at the fundus. This is not very rare, and is called *uterus arcuatus*. A more marked degree of separation is characterized by complete division of the body of the uterus by a median anteroposterior vertical septum, the cervix being normal. This form is known as *uterus bicornis unicollis*. In still more pronounced separation, called *uterus bicornis duplex*, the uterus is divided throughout its entire length by a central partition, so that there are two separate uterine cavities. The horns of such uteri are distinctly divergent; the vagina is usually normal. The most marked condition is *uterus bicornis duplex separatus*, and is characterized by complete separation of both uterus and vagina by a median septum or partition, there being two vagina and two uteri .

Atresia of the uterus is closure or obstruction of the internal or external os. It is sometimes congenital, sometimes acquired. In the latter case it may depend upon inflammatory swelling of the cervix or upon cicatricial union of the tissues of the cervix in cases of ulceration, laceration, etc., with loss of the epithelium.

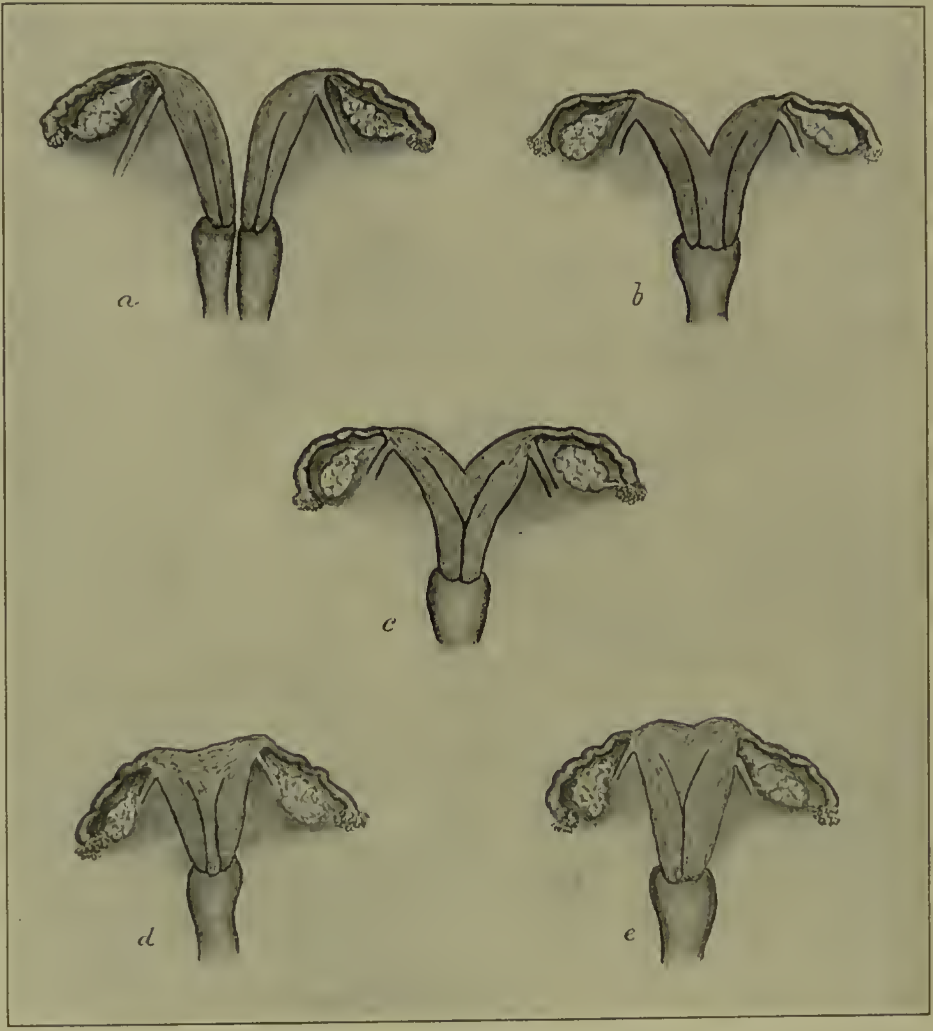

FIG. 313.—*a*, Uterus didelphys; *b*, uterus bicornis; *c*, uterus bicornis unicollis; *d*, uterus duplex septus; *e*, uterus subseptus unicollis (Beyea).

When the obstruction is congenital or depends upon causes that operate in early life, no particular results are observed until about the time of puberty, when the menstrual function apparently does not develop. In reality menstruation does occur, but the blood is prevented from escaping by the cervical obstruction and collects in the uterus. In the atresic conditions of middle life the same is true: the menstrual blood is retained and collects within the uterus, causing it to distend into a large blood cyst or *hematometra*. Immense collections of blood amounting to a number of liters are thus formed and the uterus greatly distended. The walls of the organ are usually rather thick. The retained bloody fluid is thick, gelatinous, dark red, and clear.

If the obstruction be at the external os, the uterus becomes spheric in shape; if at the internal os, pear shaped. If the external os be closed and the internal os rigid, an hour-glass enlargement may be observed.

Atresia may terminate in rupture of the uterus and the discharge of its contents into the abdominal cavity, the bladder, or the rectum, to one of which the uterus has previously become adherent. Rupture into the peritoneum is usually fatal; rupture into the bladder or rectum results in the liberation of the retained blood and the establishment of a fistula.

When, as sometimes happens, atresia develops in the postmenstrual period as a result of catarrhal inflammation, etc., a watery accumulation slowly occurs and a *hydrometra* is formed. The obstruction in these cases is usually at the internal os; the accumulation is usually not very great, and the uterine wall is thinned.

In rare cases of retained fluids decomposition occurs from the accidental entrance of bacteria, and may lead to the production of gas—*physometra*. The occlusion of the os uteri sometimes depends upon persistent inflammatory disease, as tuberculosis, etc., and leads to distention of the uterine cavity with pus. This condition is called *pyometra*.

Malposition of the uterus is an important pathologic condition. The displacements usually consist of angular flexions in the body of the uterus, or upward, downward, forward, or backward dislocations, these latter being readily permitted by the uterine attachments and probably all being modifications of the physiologic movement of the organ to escape the pressure of a distended bladder or rectum. The attachments of the broad ligaments make lateral displacements of the uterus almost impossible.

Anteflexion of the uterus is sometimes congenital, sometimes acquired. It is usually seen in virgins, though sometimes in women who have borne children. It is characterized by the formation of an angle at the junction of the neck and body of the uterus—about the position of the internal os, the open part of the angle being in front. The angle may be acute. The cause cannot be determined in many cases, but it may depend upon nutritive disturbances in the uterine wall. It may sometimes depend upon the presence of neoplasms. Anteflexions are clinically marked by vesical symptoms depending upon the pressure of the body of the uterus upon the bladder, and dysmenorrhea resulting from obstruction of the outlet of the uterus by the kink.

Anteversion is forward displacement of the body of the uterus without change in its shape, the body of the organ falling forward, the cervix backward. It usually occurs in multiparæ, and seems to depend upon a relaxed condition of the ligaments and neighboring tissues.

Retroflexion, the analogue of anteflexion, signifies a backward angulation of the uterus, which takes place near the internal os and permits the fundus to fall downward and backward toward Douglas' pouch.

Retroversion, strictly speaking, means backward displacement of the uterus without angular deformity. As the fundus falls backward, the cervix usually ascends forward. Although any one of these conditions may occur independently of the others, they are, as a rule, combined, so that it is extremely common to observe retroflexion with retroversion. This brings the fundus of the organ into the rectovaginal pouch, and causes it to press upon the posterior wall of the vagina. All grades of the condition exist, the mild degrees probably causing no symptoms, the exaggerated cases usually being associated with rectal troubles and pelvic discomfort.

The exact cause is usually not discoverable. Constipation, uterine relaxation, and malnutrition after parturition are probably frequent causes. Neoplasms often cause both retroversion and retroflexion. Lateral displacements of the uterus may depend upon congenital malformation, as in cases of *uterus unicornis obliquitas*, congenitally short broad ligament, and inflammatory disease of the broad ligament with adhesion. The lateral deviation is usually associated with retroversion.

Elevation of the uterus (*elevatio uteri*) is comparatively rare and is always a secondary process resulting from upward pressure of tumors, etc., in the pelvis, or upward tugging from large extrapelvic tumors, fibrous bands, etc. When the uterus is considerably elevated, the vagina is elongated.

Descent of the uterus, prolapsus, or **procidentia** is of frequent occurrence and gradual development. It seems to result from general relaxation of the supporting tissues and from enlargement of the uterus from congestion or other causes. The descent occurs into the vagina, which, as the uterus gradually becomes lower and lower, is invaginated and inverted.

Slight degrees of descent are spoken of as prolapse or *simple sinking;* more marked degrees, as *incomplete descent,* and the extreme degrees, *complete descent.* In the complete descent, or *procidentia,* the uterus, having descended the entire length of the vagina, appears at the vulva (*ectropion*), surrounded by the inverted vaginal tube. The orifice of the os is usually directed posteriorly, and the cervix is commonly the seat of mechanical injuries and erosions. Endometritis with marked uterine mucous discharge is usually present. The vaginal mucous membrane is much thicker than normal and may become horny.

Uterine procidentia is rarely a simple process, and, especially where inflammatory adhesions have formed, portions of the bladder (*cystocele*) or of the rectum (*rectocele*) are tugged upon by the uterus and drawn with it into the sac.

Inversion of the uterus is an accident which sometimes occurs during labor, or from combined atrophy of the uterine wall and the pressure of neoplasms. It consists in invagination of the uterus into itself, so that the entire body of the organ projects through the os with the endometrial covering outside and the serous covering inside. Inversion is sometimes accompanied by more or less complete descent of the uterus, so that the inverted organ projects from the vulva. The condition can occur only in great relaxation combined with pressure and contraction. Sometimes it is caused by traction upon the umbilical cord in the effort to extract the placenta, or by too marked downward pressure in Credé's method of extracting it.

Atrophy of the uterus is constant in old age, provided no diseased condition be present to prevent it. The uterus becomes small, pale, dense in consistence, and is found to have an enlarged cavity that not infrequently contains considerable mucus. In senile atrophy the endometrium as well as the muscular structure suffers and its glands may largely disappear.

The atrophy is physiologic, and does not come on until the climacteric is passed. It is supposed to depend upon local anemia from vascular changes. Physiologic atrophy of the uterus is also observed during the puerperium when the hypertrophied organ is reduced in size by *involution.* The retrogressive changes occur in the muscle-fibers chiefly, but also affect the vessels, the connective tissues, and the endometrium. According to measurements made by Kölliker, the reduction is not only in number, but also in the size of the muscular elements, which are reduced from 0.12μ to 0.03μ in the three weeks following labor. The reduction in size is chiefly by fatty metamorphosis of the muscle-fibers. The process is complete in about four months (Birch-Hirschfeld), though the occurrence of metritis and endometritis may delay it. In some cases the involution goes on to an extreme degree, and instead of bringing the uterus to its normal size, continues to reduce it more and more until it becomes as small as the senile uterus, and loses the greater part of its muscular tissue. In some cases the reduction in size is so great as to cause the condition to be described as *hyperinvolution* or *disappearance of the uterus.* It is likely to follow frequent pregnancies at short intervals. Pathologic conditions that predispose to atrophy are chiefly associated with pressure and deformity, such as result from morbid growths, inflammatory bands, etc. Chronic catarrhal endometritis and tuberculosis of the endometrium are said in many cases to be followed by atrophy.

Hypertrophy of the uterus may be general or local.

General hypertrophy is of rare occurrence, the majority of enlarged uteri being due to inflammation or neoplasms. During pregnancy the uterus undergoes a true simple and numerical hypertrophy, with considerable increase in size and great increase in the number of the muscular elements. The vessels and the endometrium also greatly increase in size.

Local hypertrophy of the uterus usually affects the cervix, and varies in the appearances presented. It may affect one or the other lip of the cervix, producing an asymmetric enlargement, or may affect the entire portio vaginalis, causing it to descend into the vagina. In some cases the uterus prolapses; in others it remains normally fixed and the enlarged cervix continues its growth and descent until it fills the vagina and projects from the vulva as a cylinder which much resembles a penis with a central opening—the os. Sometimes the condition is mistaken for prolapsus. At other times the supravaginal portion of the cervix hypertrophies and descends, pushing the vagina before it ; or perhaps it is pulled down by a prolapsed vagina. In cases of this kind the bladder and the rectum may also be tugged upon and prolapsed.

Hypertrophy of the supravaginal portion of the cervix is said to be more frequent than of the portio vaginalis. Hypertrophy of the median portion of the cervix may follow prolapse of the anterior vaginal wall. The hypertrophied anterior lip presses upon the anterior wall of the vagina, forces it downward and backward, and produces a diverticulum of the posterior wall of the bladder. The enlarged posterior lip of the cervix in these cases is generally found in the vagina, and covered by the prolapsed vaginal wall.

Degenerations.—Fatty metamorphosis of the muscular tissue of the uterus is seen in very severe infections, especially in typhoid fever and cholera, and in certain intoxications, notably by phosphorus. This form of degeneration also occurs during involution after parturition, being then physiologic.

In fatty metamorphosis the uterus is of a grayish-yellow color, of soft, flabby, lacerable consistence, and is sometimes marked by punctate hemorrhages.

Amyloid disease is rare. When it affects the muscle-fibers, it causes the uterus to become large, pale, and translucent. It may affect the vessels of the organ without invading the muscular tissue. The characteristic iodin reaction will determine the extent of the lesion.

Anemia of the uterus seems to be comparatively unknown except in senile endarteritis associated with senile atrophy. One might almost say the uterus was normally anemic, so pale is its structure and so meager its blood-supply.

Hyperemia of the uterus may be active in the early stages of menstruation and in pregnancy. The uterus is enlarged, softened, rich in blood, and contains injected vessels on the surface. The secretion of the endometrial glands is usually increased. Reflex conditions and malpositions also cause hyperemia of the uterus.

Hyperemia or Congestion of the Endometrium.—This condition, which is pathologically characterized by the presence of an unusually active blood-supply, is clinically characterized by a thin, serous, seromucous, and sanguinolent discharge. When chronic and the glands much hypertrophied, there may be typical leukorrhea. The condition is in all probability somewhat akin to menstruation, in that the endometrium is thickened, its blood vessels distended, its substance infiltrated with serum and blood, and its glands stimulated to unusual activity. The escape of blood corpuscles probably takes place by diapedesis. The discharge occasioned is varied according to the degree of glandular activity, the amount of transudation, and the diapedesis of corpuscles. When fragments removed by the curet are examined microscopically, the surface membrane is unaltered, the glands normal or enlarged, the stroma irregularly infiltrated with blood corpuscles, and numerous leukocytes in the interstitial tissue, wandering to the epithelium at times and even insinuating themselves between the cells so as eventually to reach the surface. In very chronic cases there may be hyperplasia of the endometrium, multiplication of the glands, and polypoid excrescences of the mucous membrane ; or, as in other chronic congestions, there may be changes of an atrophic nature.

Etiology.—The causes of hyperemia are numerous. The congestion may depend upon such physiologic causes as result from natural or unnatural stimulation of the sexual organs ; or it may depend upon reflex causes, as in diseases of the adnexa with congestion of the uterus. Uterine displacements and neoplasms may also become causes of uterine congestion by preventing the proper return of the venous circulation, and by increasing the arterial circulation, as in cases of interstitial fibroids, which act like pregnancy in increasing the size of the uterine sinuses, and in submucous fibroids, which, by stimulating the uterus to contraction while increasing its size, cause it to make powerful expulsive efforts.

Congestion and the serosanguinolent discharge which it occasions are predisposing factors to infection when any possible occasion arises. When, however, bacteria begin to operate upon the endometrium, the condition changes and becomes an inflammation instead of a hyperemia. When, as usually happens, the bacteria cease their operations, after a time the original condition may return with such modifications as the destruction of tissue, etc., shall effect.

To congestion of the endometrium must be referred those cases of continuous bloody discharge from the uterus which occur during the climacteric.

These cases may depend upon causes situated within the spinal centers and upon irregular action of these centers in performing a function about to be suspended. The cause of menstruation is, of course, not determined, but it surely does not depend upon causes resident within the uterus, as it ceases when the ovaries are removed. It is, therefore, involved in some complicated nervous reflex mechanism associated with both organs. The ordinary periodicity of menstruation depending upon a proper operation of such mechanism, one can understand how irregular action of the apparatus may entirely check the menstrual flow, or maintain it indefinitely, and is, therefore, prepared to expect that when it is about to cease altogether, it may continue intermittently for a time.

In rare cases profound general anemia may be associated with a discharge from the uterus which is of a mucous or mucopurulent nature. This probably depends upon a hydremic condition of the blood, which, no longer stimulating properly the nervous controlling apparatus of menstruation, still supports glandular activity and enables the uterine glands to continue an exalted activity.

Passive hyperemia is seen in pronounced malposition, neoplasms, etc., producing obstruction of the venous channels. It may also occur in heart disease. The organ is enlarged, enlarged veins appear on the serous surface, and the mucosa is reddened. Hemorrhagic exudates occur from the endometrium, which is usually hyperplastic and its glands enlarged.

Hemorrhage.—Hemorrhage from the uterus is physiologic at the menstrual periods, and most of the pathologic hemorrhagic conditions of the organ are associated with modifications or alterations of this function. Thus, when the menstrual periods are prolonged and the quantity of blood lost is increased, the condition is described as *menorrhagia*. It depends upon a variety of conditions, most of which are associated with congestion of the uterine walls and endometrium, those of most usual occurrence being inflammation, malposition, and neoplasms. When menstruation is associated with pain, the condition is called *dysmenorrhea*. Dysmenorrhea and menorrhagia are frequently combined.

It was at one time thought that at the menstrual periods the entire uterine mucous membrane was destroyed by the bloody infiltration, and that after each period a complete regeneration took place. This view is not compatible with modern investigations upon the subject, and it is doubtful whether menstruation under normal conditions results in any loss of endometrium. Under pathologic conditions, however, the endometrium is occasionally separated and discharged in bits and shreds, which appear in the flux. Such cases are known as *dysmenorrhœa membranacea*. Sometimes a pseudomembranous inflammatory condition is seen, in which fibrin is disposed as a surface layer upon the endometrium. Rarely, when examined microscopically, the bits of membrane are found to consist of stratified squamous epithelium, probably from the portio vaginalis of the cervix.

Metrorrhagia is a bloody flow from the uterus occurring independently of menstruation. Thus, after the menopause a bloody discharge may occur and persist, or during sexual life there may be occasional intermenstrual hemorrhages, or a constant persistent flow intensified at menstruation. Metrorrhagia depends upon both constitutional and local causes. Of the former, may be mentioned hemophilia, scurvy, and various infectious diseases; of the latter, inflammations and neoplasms.

Interstitial hemorrhage of the uterus may result from traumatism. Sometimes in senile uteri with rigid arteriosclerotic vessels rupture occurs and is followed by the formation of a *hematoma*. This blood cyst is usually situated in the posterior wall of the uterus.

Blood sometimes escapes from the surface of the uterus in perimetritis and collects in Douglas' pouch, forming what is known as *hæmatocele rectouterina*. Sometimes it enters the vesico-uterine excavation, forming *ante-uterine hematocele*. More rarely the escaping blood dissects its way between the layers of the broad ligament.

Inflammation of the Uterus.—For convenience of study it is best to consider the inflammatory affections of the uterus as affecting its lining mucous membrane—*endometritis*; its proper muscular structure—*metritis*; and its serous covering—*perimetritis*.

Inflammation of the Endometrium.—*Acute Endometritis.*—This is a comparatively rare affection resulting from the activity of bacteria. Those usually seen are the gonococcus and Streptococcus pyogenes. The disease is acute and accompanied by a purulent discharge from the uterus.

Acute endometritis is not always occasioned by local infection, but at times occurs in the course of typhoid fever, cholera, scarlatina, and diphtheria. Diphtheritic endometritis caused by the true Klebs-Löffler bacillus is also known. It is, however, probably extremely rare except in infections following childbirth and abortion.

Birch-Hirschfeld states that an acute endometritis occurs in the course of certain toxemias, such as poisoning by phosphorus, etc. It is, however, more than probable that instead of a true acute inflammation, it is a degeneration.

Traumatic injuries by instruments, foreign bodies, etc., whether septic or not, produce an acute endometritis.

Morbid Anatomy.—The morbid anatomy of acute endometritis is simple and interesting. The membrane is swollen, hyperemic, and ragged from desquamation of its superficial layers. The surface is bathed with a thick, purulent or mucopurulent secretion. Small hemorrhagic patches are described by some observers. The disease is usually much more distinct at the upper part of the uterus than at the cervix, and may be described as corporal endometritis. Both the corpus and cervix may be affected.

Microscopically the lesions consist of round-cell infiltration of the stroma, desquamation of the surface epithelium, and exudation of corpuscles upon the surface of the membrane. The pus-corpuscles are found in larger or smaller numbers everywhere. They crowd the interspaces of the glandular stroma, squeeze between the cells of the surface and glandular epithelium, not infrequently enter the cells themselves, where they appear to be contained in vacuoles, and, by escaping from between the glandular cells, enter their secretions, so that they have a mucopurulent character before they leave the alveoli.

The bacteria causing the trouble are found only in the beginning of the proeess. Secondary infections with modifications may occur at any time.

Acute endometritis usually runs a course of moderate duration, with a tendency to spontaneous recovery. From the acute cases, however, by persistence of the cause, by structural alterations, and because of nutritive disturbances, slightly different subacute and chronic processes may develop.

Chronic Endometritis.—Chronic endometritis can probably be diagnosticated only by careful exclusion of other pathologic conditions. It is probably not of frequent occurrence, though nearly every uterine condition with a discharge has been called by this name.

As has been said, the disease follows the acute form when the cause of inflammation persists. It is occasioned by foreign and retained bodies in the uterus, also by secondary affections engrafted upon congestion of the uterus and endometrium. As a diseased condition, there is nothing distinctive about it, and its lesions are very atypical.

In the early stages there is some round-cell infiltration, showing that the process has originally been acute. There is little hyperemia, yet the blood vessels are full, and there may be some extravasation of blood. The glands are prone to hyperplasia or hypertrophy (*glandular endometritis*), and pour into the cavity of the organs a considerable quantity of viscid, slightly purulent mucus. Obstruction of the glandular outlets is followed by cystic dilatation. There may be signs of connective-tissue hyperplasia in the glandular stroma. As in other forms of chronic inflammation of mucous membranes, there may be occasional papillary or polypoid excrescences upon the surfaces of the membrane.

The course is indefinite, and there is no tendency for spontaneous cure.

In the very chronic cases an atrophic condition results from the connective-tissue proliferation and contraction, by which the glandular tissue, being pressed upon, gradually atrophies (*interstitial endometritis*). In this form there is a rather frequent obliterative endarteritis, by which a considerable number of vessels are destroyed.

Metritis is probably always of infectious origin. Inasmuch as the opportunity for the occurrence of infection is far greater during the puerperium when involution of the uterus is in progress, the passages occupied by putrescible matters, and the position of the placenta denuded and open for the entrance of bacteria, the greater number of cases occur during that period.

Etiology.—*Acute metritis* may depend upon puerperal infection or upon gonorrheal infection; or may follow traumatic damage done the tissues by gynecologic instruments, etc. It may depend upon endometritis.

Morbid Anatomy.—The uterus is enlarged, congested, soft, plastic, and infiltrated with the inflammatory exudate. Microscopically, the chief changes are observed along the blood vessels and lymphatics, where a round-cell infiltration, more or less marked, can be observed. Here and there small abscesses may be seen. The muscle-cells may show signs of degeneration. In exaggerated cases of puerperal metritis gangrene of the tissues may occur. Thrombosis of the uterine sinuses and veins is common, and suppurative lymphangitis is frequent in and about the organ.

Chronic metritis is usually the result of the acute form of puerperal metritis. In the early stages the uterus is enlarged. Along the blood vessels occasional round-cell infiltrations and growing connective tissue may be found. As the disease progresses a greater amount of connective tissue is formed in the intermuscular septa and about the vessels, and by its contraction presses upon the muscular substance, which atrophies. The outcome of the process is a small, firm, dense, and pale uterus. The peritoneal covering is usually thickened from chronic perimetritis.

Occasionally the process chiefly affects the cervical part of the organ, so that it and the os become greatly swollen, elongated, and enlarged. The tissue is soft, congested at first and indurated later on, and is easily mistaken for carcinomatous infiltration. This condition is sometimes called *infarction of the os uteri*.

Perimetritis is a local form of peritonitis which affects the serous covering of the uterus. It occurs as a result of puerperal infection, traumatic injury, rupture of the uterus, neoplasms, pyosalpinx, salpingitis, oöphoritis, etc. It may be acute or chronic, the greater number of cases probably being chronic in course. The acute stage is frequently characterized by a pseudomembranous exudate that may partly or entirely cover the uterus. In the more wide-spread cases, more correctly described as *pelveoperitonitis*, this exudate extends like an icing over the uterus, ovaries, tubes, broad ligaments, and neighboring tissues.

The exudate consists at first of fibrin, but is soon replaced by granulation tissue and the original agglutinations which form between neighboring tissues and give place to firm fibrous adhesions. These adhesions are more numerous and dense posteriorly than anteriorly, and very often obliterate Douglas' pouch. Displaced or prolapsed organs entering the inflamed territory become adherent, and not infrequently the pelvis is filled with a mass of organs and tissues so intimately adherent as to be with difficulty dissected apart, the whole mass covered with a smooth shining covering like an icing.

Parametritis is a name given by Virchow to inflammations, usually acute in origin, which occur chiefly during the puerperium or after traumatic or deep ulcerative lesions of the uterus. They originate in the uterus and upper part of the vagina, and extend to the broad ligaments and pelvic cellular tissue; sometimes to the retroperitoneal cellular tissue and to the iliac fossæ and lumbar region; rarely over the bladder and lower anterior abdominal wall.

Ulceration of the cervix uteri usually occurs at the vaginal portion, upon the surface covered with squamous epithelium.

Erosion of the cervix usually results from catarrhal or gonorrheal endometritis and the escape of the irritating discharges from the os upon the vaginal surface. Lisfranc has observed the erosions occurring in consequence of herpetic eruptions. The lesion consists in circumscribed areas of denuded tissue, usually excentrically situated, and often not extended to the os. The ulcer is a simple one, its base consisting of denuded tissue infiltrated with leukocytes.

Granular erosion is a term properly applied to simple erosions or ulcers with large granulations upon the surface. According to the observations of Fischel and the views of Cullen, this term should be restricted to cases in which no actual erosion or ulceration is present, but in which because of previous ulceration or inflammation an abnormal relationship between the endometrium and cervical squamous epithelium has occurred and the endometrium with its columnar epithelium and glands has grown down and out upon the surface formerly or normally covered by squamous epithelium—a form of metaplasia. This condition is always concentric—that is, the eroded area surrounds the os uteri.

Clark's phagedenic ulcer of the cervix is a rapid loss of substance of the cervix, extending to the bladder and sometimes to the rectum, the tissue undergoing necrosis and separating slowly. It was thought at one time to be carcinomatous, but repeated attempts to prove it have failed. The surrounding tissue is not inflamed.

Traumatic Injuries of the Uterus.—Traumatic lesions of the uterus may result from bodies developed within the uterus, as fetuses and neoplasms; or from various objects accidentally or intentionally introduced from without for purposes of operation or for the production of abortion.

The instrumental lesions usually consist of incisions, lacerations, or punctures. They may be followed by perfect recovery in aseptic operations, such as Cesarean sections, myomectomy, etc.; or may be followed by local or fatal peritonitis in cases where, through accident or carelessness, the perforation has been the means of conveying micro-organisms to the peritoneum.

Of the injuries inflicted, the most frequent are lacerations of the vaginal portion of the cervix during the passage of the fetus through its canal, or sloughs following prolonged pressure upon the soft parts by the resisting fetal head.

The **lacerations of the cervix** do not readily heal, and the gaping surfaces become covered by spongy or exuberant granulations, so as to produce angry-looking, red, granular ulcerations. These lesions were always considered ulcerations of the cervix before their true nature as gaping fissure was pointed out. In chronic cases there are always considerable inflammation, swelling, and thickening of the vaginal portion of the cervix. Very chronic cases eventually may recover by the formation of large dense cicatrices. The lacerations vary greatly in appearance and may be simple, double, multiple, or stellate.

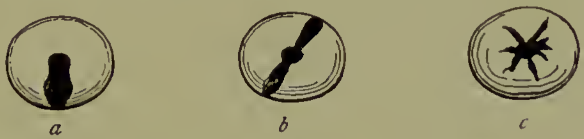

FIG. 314.—Varieties of lacerations of the cervix uteri: *a*, Simple; *b*, double; *c*, multiple or stellate.

The pressure sloughs of the soft tissues that result from detention of the head in its passage through the pelvis, as well as occasional lacerations down to the soft parts by the obstetric forceps, frequently terminate in *fistulæ* or *urogenital fistula*.

Urogenital Fistulæ.—These are named according to the cavities they connect. Thus a fistula between the vagina and bladder is called a *vesicovaginal fistula;* one between the vagina and rectum, a *rectovaginal fistula*. In this manner may occur *rectovesical, vesico-uterine, uretero-uterine, recto-uterine, recto-ureteral, urethrovaginal, vesico-uterovaginal*, and other fistulæ. The abnormal communication permits the passage of the contents of one viscus into another with annoying, injurious, or even fatal results. Thus, in vesicovaginal fistula the urine escapes from the vagina and soils the clothing and excoriates the tissues. In rectovesical fistula fecal matter enters and infects the bladder. In recto-ureteral fistulæ the infectious contents may enter the ureters and be carried to the kidneys, where they occasion fatal infection.

Tuberculosis of the uterus is a rare affection usually affecting the endometrium. It is, in most cases, secondary to tuberculosis of the tubes. It may, however, be primary, the possibility of direct infection during coitus always suggesting itself. Endometrial tuberculosis is sometimes observed in childhood.

The entire endometrium may eventually be destroyed and transformed into a yellowish-white, cheesy mass. The os uteri is sometimes closed, and the uterus dilated with a collection of cheesy pus—*pyometra*. Outlying tubercles may be found in the muscular substance of the organ. Rare cases of tuberculosis of the cervix are sometimes observed.

Syphilis of the uterus is not common. The primary lesion or chancre is sometimes situated upon the portio vaginalis of the cervix, such chancres being more frequent upon the anterior than upon the posterior lip of the cervix. The ulceration is sharply circumscribed and has infiltrated borders and a brawny base. The lesion heals with the formation of a dense stellate scar. Erosions of the uterus depending upon irritating discharges are very frequent. *Gummata* sometimes form in the uterine wall, and diffuse chronic endometritis is common. Birch-Hirschfeld suggests that this syphilitic endometritis is a probable cause of the syphilitic disease of the placenta.

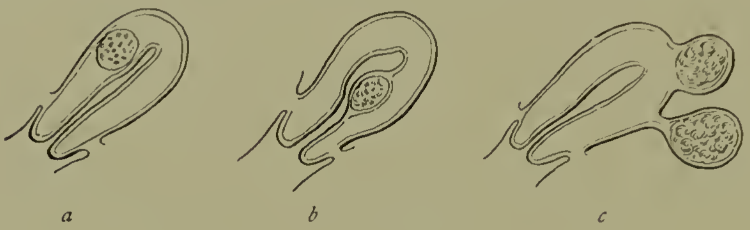

FIG. 315.—Fibroid tumors of the uterus: *a*, Intramural; *b*, submucous; *c*, subperitoneal.

Tumors of the Uterus.—Fibroid.—This very common tumor, usually spoken of as a *fibroid* tumor, is almost invariably a muscular tumor with little admixture of fibroconnective tissue. It would be correct to speak of it as a *fibromyoma*, and in many cases it is a pure *leiomyoma*. Ziegler, however, mentions pure *fibroma* of the uterus. The tumors occur at all ages and in all races, the negro probably being more predisposed to them than the Caucasian. They may be as small as a pea, or weigh 50 pounds or more.

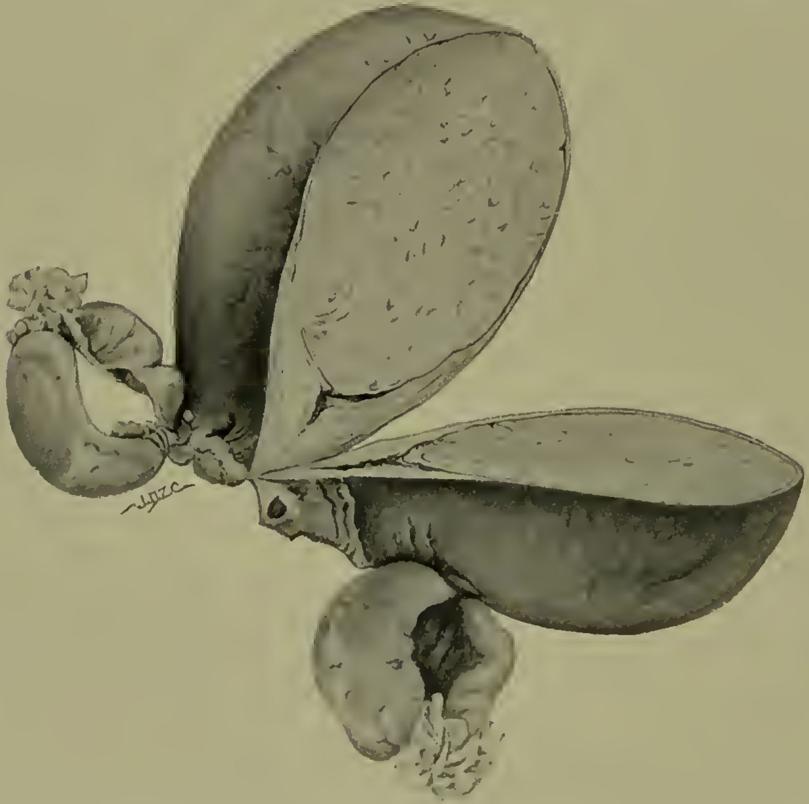

FIG. 316.—Submucous fibroid in the uterus. The tumor forms a large mass in the interior of the organ whose wall is much attenuated at the fundus. The cervix is nearly normal in size, though somewhat altered in shape. The ovaries and tubes which are still attached are normal.

The tumors may be situated in the muscular body of the uterus, when they are said to be *mural*, *intramural*, or *interstitial;* beneath the endometrium, where they are called *extramural* or *submucous;* or beneath the peritoneal covering of the uterus, *extramural* or *subperitoneal.*

By increasing in size the mural fibroids may cause the greatest imaginable deformity of the uterus, several of them so altering its shape at times as to make it unrecognizable when removed from the body.

The submucous fibroids are usually situated posteriorly at the fundus. They rarely attain very large size because of the contraction their presence stimulates and the looseness of their attachments which predisposes to ready detachment and removal. They are sometimes called *fibrous polyps.* Such tumors may be "born" entire, and spontaneously, or may be withdrawn by forceps. They may detach from the uterine wall without escaping from the uterine cavity, remaining to calcify and form *uteroliths* or loose calcareous bodies in the organ.

The largest fibroids are subperitoneal, as their growth is neither limited by the cavity in which they grow, their removal facilitated by contractions, or their tissue surrounded by the unyielding uterine wall. The only limit placed upon the growth of a subperitoneal tumor is the likelihood that it will outgrow the nutriment supplied through its pedicle. That this nutriment is likely to fail is made certain by the fact that the vessels are usually small, that they are not at all numerous in the tumor, and that fibroid tumors are commonly calcified, ossified, or have undergone mucous degeneration.

The formation of the pedicle depends upon traction upon the tissues made by the tumor as it projects from the uterine wall. It consists of a small amount of muscular tissue, some vessels, and peritoneum. In cases where the pedicle is long, it is likely to become twisted and interfere with the nourishment of the tumor, and by becoming more and more attenuated, the possibility of rupture increases. This accident is not uncommon and results in the formation of a *free body* in the abdominal cavity. The freed tumor may be slowly absorbed or may calcify. In some cases before rupture of the pedicle the growths become adherent to neighboring organs from which they derive nourishment through the vascularized adhesions.

The cysts in fibroid tumors may be formed by degeneration and softening of the tissues, though they sometimes depend upon lymphangiectasis.

Fibroid tumors often exist for a long time without the knowledge of the patient. The submucous fibroids call attention to their existence by the occurrence of menorrhagia and metrorrhagia resulting from the hyperemia occasioned by their presence. They sometimes become infected and may suppurate or even become gangrenous. Interstitial and submucous fibroids complicate pregnancy by deforming the cavity of the uterus and preventing its dilatation. They may also afford obstacles to the passage of the child. The subperitoneal fibroids are least liable to attract attention, although before their size becomes very great the pressure upon the bladder or rectum may become unbearable.

Fibroid tumors are very commonly multiple. They usually occur in the corpus, very rarely in the cervix.

Lipoma of the uterus is extremely rare.

Sarcoma.—About 2 per cent. of the malignant tumors of the uterus are sarcomata. They usually arise from the connective tissue between the bundles of muscular tissue and about the vessels, but according to the researches of Van Kahlden and Williams, seem also to occur from a metaplasia of the muscle-cells (*myoma sarcomatodes*).

Sarcoma of the myometrium usually occurs in the corpus of the uterus and forms rounded nodes of varying size which are less well circumscribed by encapsulating connective tissue than the myofibroma. The color of the cut surface is grayish-white and the consistence soft and homogeneous, quite unlike the dark, fibrous, dense fibroids.

Microscopically they are composed of spindle-cells, the spindles usually being large and long. Round-cell forms have occasionally been seen. From a microscopic examination alone the diagnosis of this tumor presents many difficulties, for the cells closely resemble those of rapidly growing muscle tissue. In both tissues the cells are large spindles with oval or spindle-shaped nuclei of distinctly vesicular form. The nuclei usually stain similarly with the ordinary stains. The ends of the cells often present markings suggestive of cross-striations. There is no visible intercellular substance.

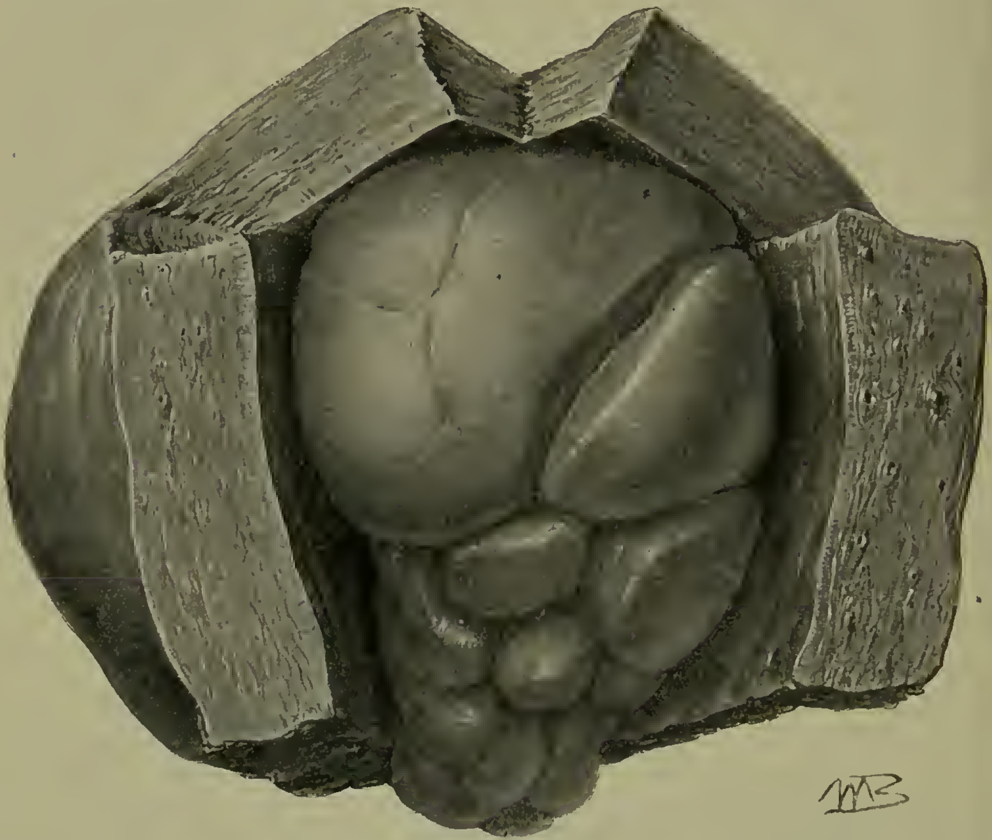

FIG. 317.—Sarcoma of the body of the uterus, secondary to that in the right ovary. The uterus is considerably enlarged. Occupying the posterior wall is a new growth which projects into the uterine cavity, forming two large and numerous smaller, sharply defined, smooth, and faceted nodules. Their shapes and relations to one another remind one somewhat of calculi. On histologic examination it is found that the surfaces of several are still covered by the mucosa, which is, of course, much atrophied (natural size) (H. A. Kelly).

Both tumors are quite avascular and are prone to undergo myxomatous degeneration. The sarcoma develops more rapidly; both tumors develop in middle life. The sarcoma, like the fibroid, may remain interstitial, or may grow in one or the other direction, becoming subperitoneal and pedunculated or submucous. The pedunculated tumors are usually nodular in appearance and sometimes distinctly lobulated. They may grow into the broad ligament. A subperitoneal sarcoma may become as large as a gravid uterus.

The theory that sarcoma of the body of the uterus occurs in consequence of sarcomatous "degeneration" of fibroids is scarcely acceptable. They usually do not give metastasis, though some cases of pulmonary secondary growths are recorded.

Sarcoma of the endometrium springs from the subepithelial tissue of the endometrium. The differentiation of this tumor from the sarcoma of the myometrium is not always possible, but the classification is useful where applicable.

Endometrial sarcomata may occur as circumscribed, sessile, or pedunculated nodes, or as diffuse infiltrations. They are likely to occur in the neighborhood of the cervical canal, and not infrequently project from the external os as good-sized, nodular, pale-colored, spongy, soft, more or less vascular, pedunculated growths. The surface is usually smooth, and may be covered with a mucopurulent layer. Sometimes the tumor is devoid of vessels and prone to extensive degeneration; sometimes it is telangiectatic. *Angiosarcoma* is rare.

The diffuse form fills up the cavity of the uterus with a whitish, spongy, seminecrotic mass, accompanied by a fetid discharge.

The endometrial sarcomata may be composed of spindle- or round-cells, and not infrequently contain giant-cells. Some of the tumors are mixed and contain both round- and spindle-cells.

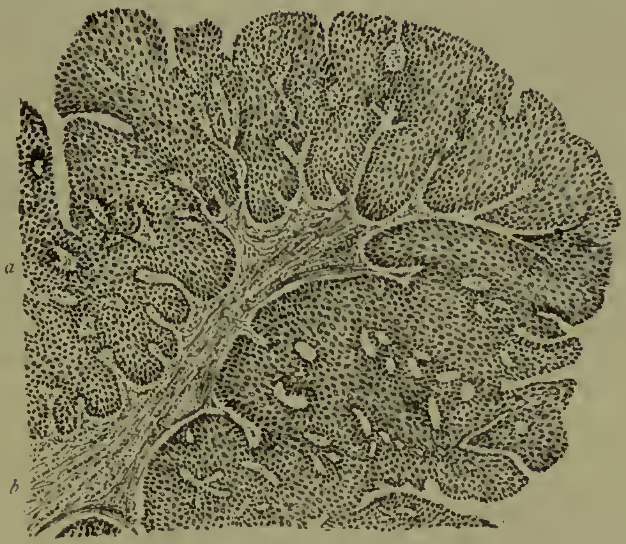

FIG. 318.—Condyloma acuminatum: *a*, Greatly thickened epithelial layer; *b*, papilla with arborescent branching (Ziegler).

In the growth of the endometrial sarcomata, endometrial glands are sometimes caught and seem to proliferate, suggesting the combination of sarcoma and adenoma. The addition of the epithelial elements is probably purely accidental, and has no special significance.

Spiegelberg's grape-like sarcoma, or *sarcoma uteri hydropicum papillare*, is a peculiar tumor observed in youth and childhood, which probably has its origin in embryonal remnants of Wolff's bodies. The tumor makes its appearance at the cervix and upper part of the vagina as a collection of rounded, grape-like or berry-like, soft, grayish bodies, which, upon microscopic examination, show round- and spindle-cells in a more or less advanced state of myxomatous degeneration. Sometimes epithelial tubules are present, sometimes islets of cartilage, sometimes smooth or striated muscular elements, so that the tumor is greatly mixed in character. It is malignant.

Papilloma of the cervix uteri is rather frequent. It appears as a pedunculated, more or less cauliflower-like growth, consisting of numerous papillæ covered with stratified pavement epithelium. It occurs chiefly in middle life, and may be multiple. It may gather the uterine discharges in its sulci, their putrefaction causing some fetor.

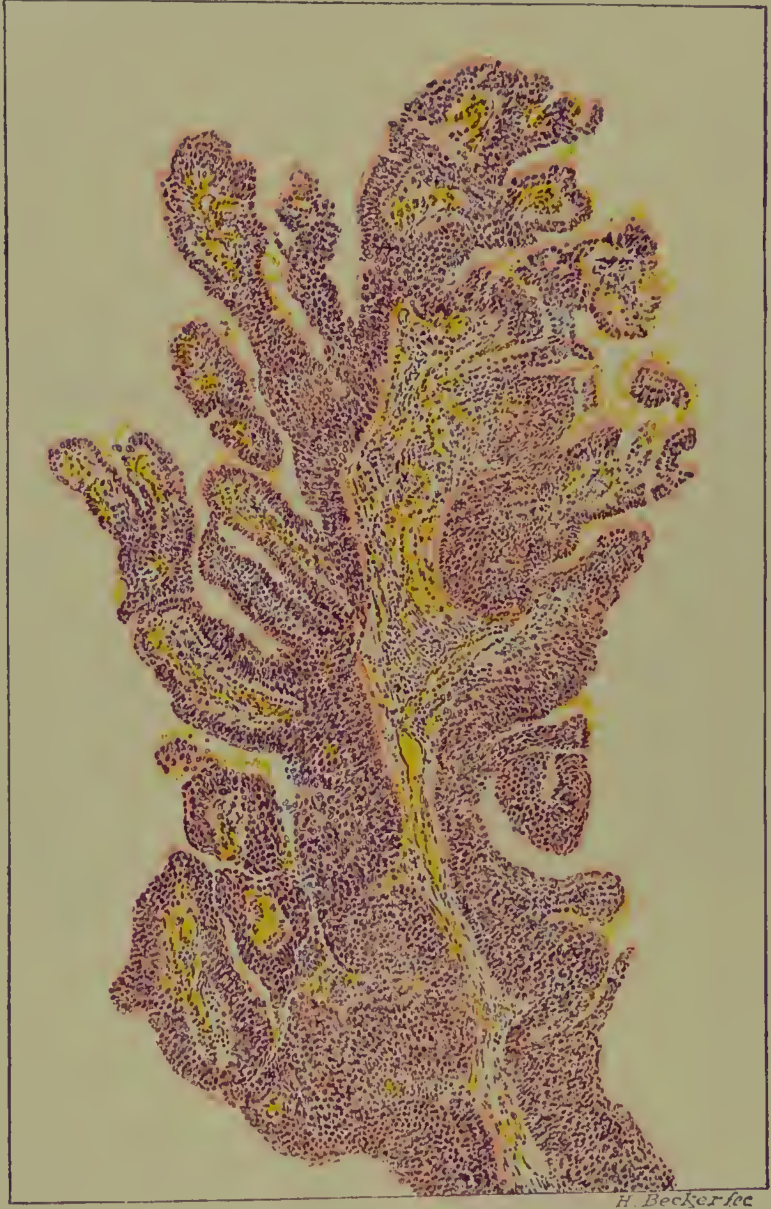

FIG. 319.—Squamous-cell carcinoma of the cervix; finger-like processes arising from a common stem. Traversing the center of the specimen is a delicate stem of connective tissue, in the center of which is a blood vessel. This stem gives off lateral branches, which likewise contain blood vessels. The main stem is covered in some places by only one layer, in others by many layers of squamous epithelium. The epithelial cells next to the stroma tend to be cuboidal. The epithelial nuclei throughout are fairly uniform in size. Near the left lower corner are several cross-sections of the terminal branches or fingers. These present a typical appearance (× 80) (Cullen).

It is not infrequent to find the tumor growing upon the wall of the vagina as well as upon the uterine neck. *As long as it is a pure excrescence it is a benign growth*, but it seems to be commonly accompanied by epitheliomatous infiltration of the cervix.

Venereal warts or **condyloma acuminata** also occur upon the neck of the uterus and vagina, but are benign in nature.

Squamous epithelioma of the cervix is the most frequent malignant tumor of the uterus. It usually appears between the thirty-fifth and fiftieth years of life, upon the vaginal surface of the cervix, not infrequently causing cauliflower-like papillary excrescences that cannot be distinguished in all cases from the simple papilloma, either by macroscopic or microscopic examination. *Clark's cauliflower growth* or *destructive papilloma* is one of the most typical forms, the excrescence from the cervix being accompanied by a more or less wide-spread epithelial infiltration of the tissues of the cervix. The excrescence may be as large as the fist, and the infiltration of the cervix slight. but after the removal of the former the latter remains and continues to infiltrate, producing a new excrescence and sometimes rapidly invading the neighboring tissues. Sooner or later the squamous epithelioma leads to the formation of ulcers which slowly and persistently increase, at the same time often developing papillary outgrowths. The tumor tissue is pinkish in color and very hard and dense. In tendency the squamous epithelioma is more locally destructive than metastatic. It infiltrates the vagina, bladder, and rectum, and occasions hemorrhage, perforation, and peritonitis.

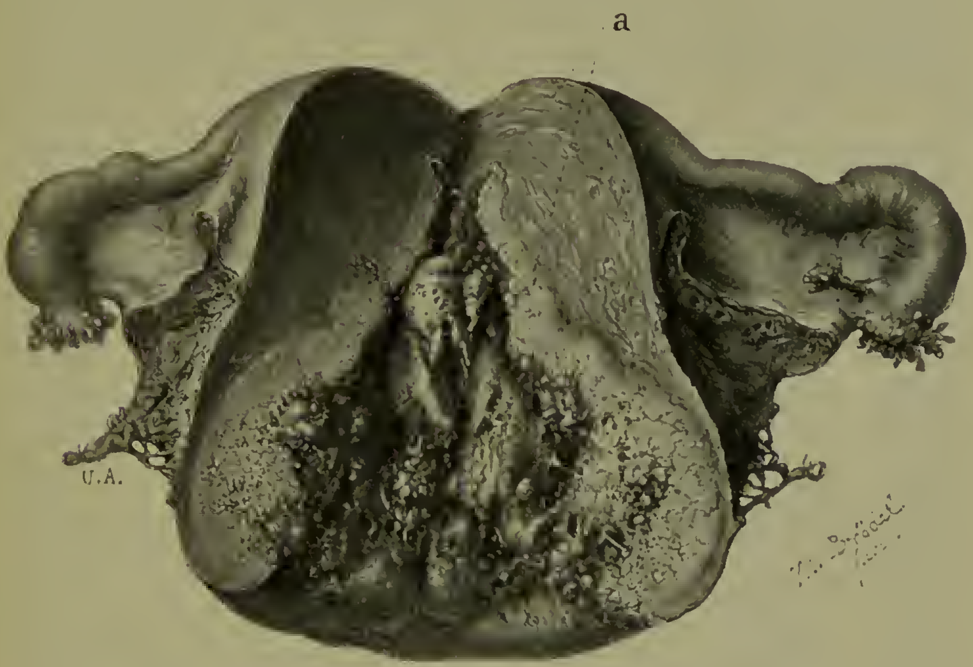

FIG. 320.—Adenocarcinoma of the body of the uterus. The cervix is greatly enlarged, but its vaginal portion is intact. Occupying almost the entire cervix and the greater part of the uterine cavity is a new growth presenting a coarsely lobulated appearance, with numerous clefts between the elevations. Springing from the surface at a few points are delicate finger-like outgrowths. Laterally, the growth has extended almost to the broad ligament attachments, and its advancing margin is sharply defined. The uterine mucosa over the area indicated by *a* is apparently still intact, but the surface is somewhat uneven. The uterine walls in the upper part of the body present the usual appearance. Laterally, the uterine arteries are seen. The body of the uterus is free from adhesions, and the tubes are apparently normal. The marked involvement of the cervix naturally suggests a cervical origin for the growth, but histologic examination proved that the majority of the cervical glands were normal, and that the type of the growth corresponded to that usually found in the body (Cullen).

Histologically, the tumor is typical. Epithelial pearls are usually absent, cases in which they occur showing unusual keratin production.

A more usual form of squamous epithelioma of the uterus arises from the portio vaginalis of the cervix, and is without the papillary growths described.

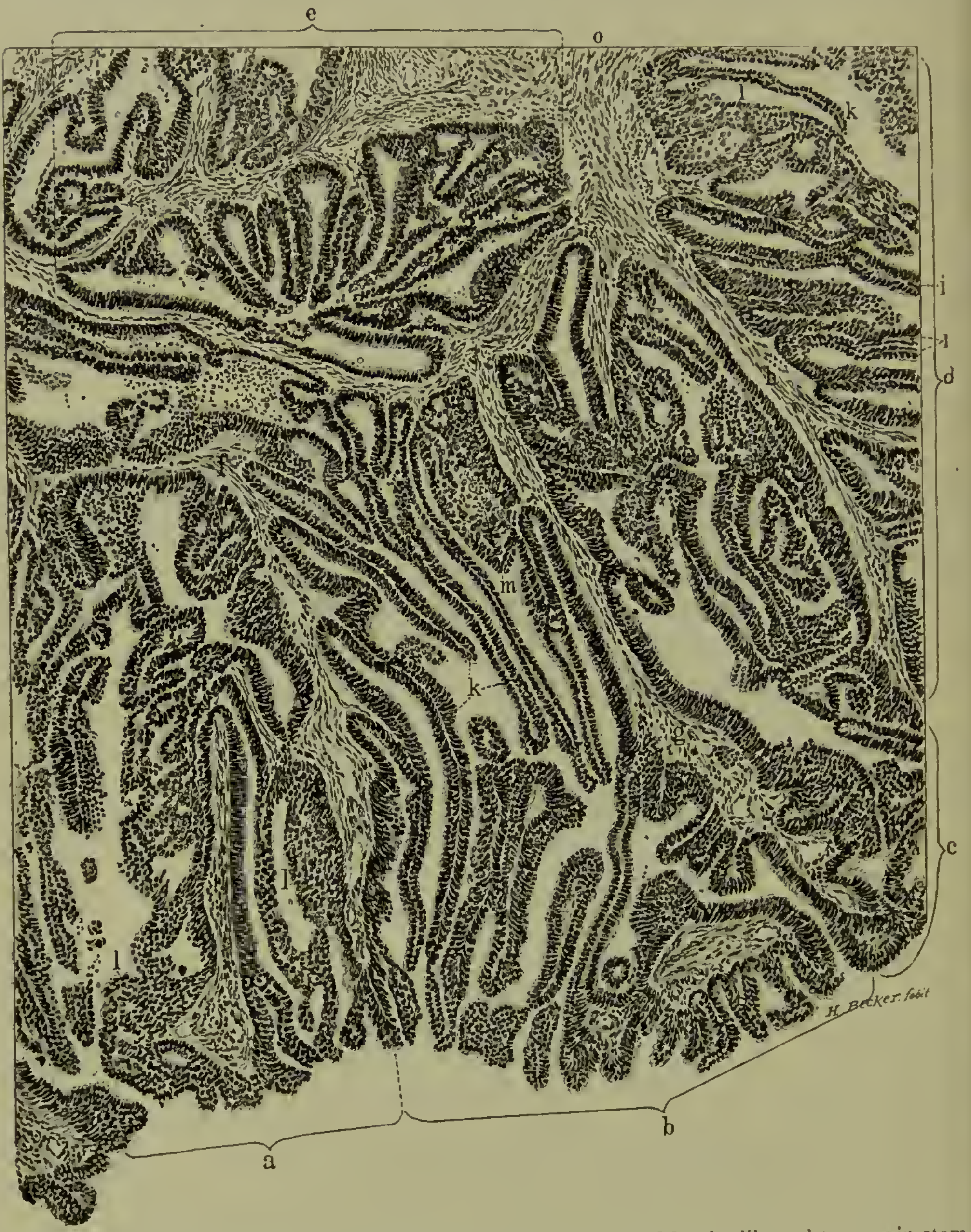

FIG. 321.—Adenocarcinoma of the body of the uterus: *o*, May be likened to a main stem from which arise numerous secondary stems, which in turn give off delicate terminals, consisting entirely of epithelial cells. The glands may be divided into groups *a*, *b*, *c*, *d*, and *e*, by the stems of stroma *f*, *g*, and *h*. The stems are covered by several layers of cylindric epithelium, while projecting into the gland cavities are long slender ingrowths of epithelium, devoid of stroma, as seen in *i*. Very delicate ingrowths consisting merely of two layers of epithelium are seen at *k* and *k*. At *l* the epithelium is several layers in thickness, and at *m* many layers with leukocytes. The arborescent character of the growth and peculiar gland grouping are characteristic of adenocarcinoma (Cullen).

It begins as a dense infiltration of the tissue, in the cervical canal, just within the external os, where the squamous and columnar transformation occurs, and in the beginning may be sharply circumscribed. The cells infiltrate the subepithelial layers of the mucous membrane, then extend into the deeper tissues. The extension of the growth is progressive, and occurs in a downward direction, appearing upon the vaginal surface of the cervix and slowly extending to the vagina. The infiltration is followed by superficial necrosis and exfoliation, and soon considerable-sized ragged ulcerations form, the surface becoming covered with fetid decomposing material. The growth extends into the peri-uterine loose cellular tissue between the uterus and bladder, and then in all possible directions, with inflammatory and subsequently neoplastic unions between the uterus and other organs, and frequent fistulous communications between the uterus, vagina, bladder, and rectum. The tumor cells also distribute through the lymphatics to the corpus of the uterus, to the iliac lymphatic glands, and later to the inguinal, crural, and lumbar glands. Hematogenous distribution is rare, and the disease remains local, producing the most wide-spread pelvic disturbance, and death through accidental hemorrhage, peritonitis, etc., rather than by generalization.

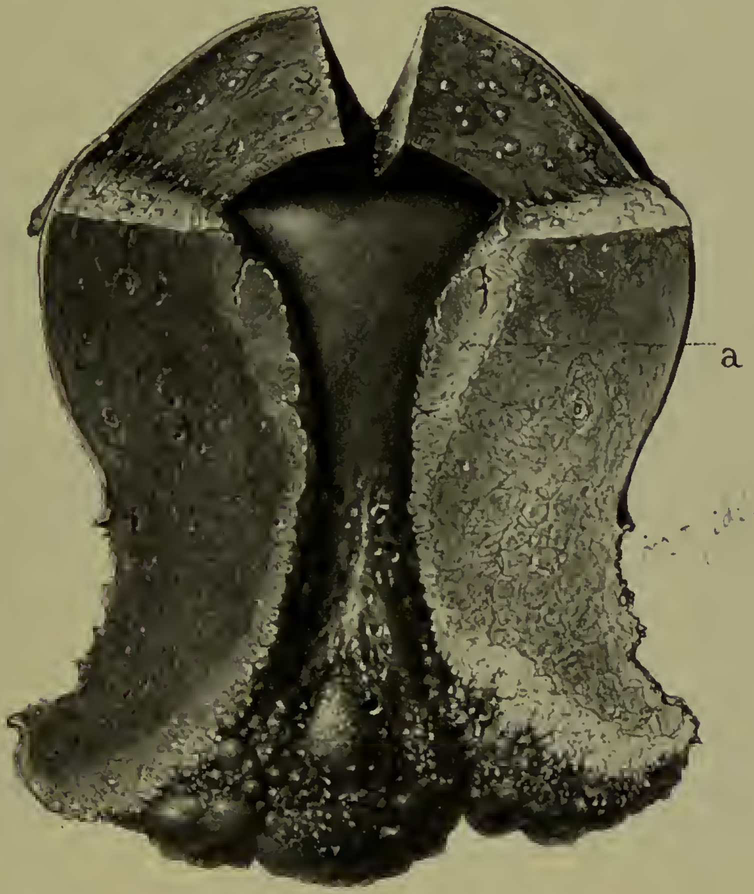

FIG. 322.—Adenocarcinoma of the cervix with extension to the polyp (*a*) and to both uterine horns. The cervix is considerably enlarged, and presents a rough, uneven surface, due to dome-like elevations varying in size from a pin's head to 5 or more millimeters in diameter, between which are a few finger-like projections. The growth has apparently penetrated the cervix for a distance of from 2 to 10 millimeters, and on one side has advanced almost to the cut surface. The cervical mucosa, near the internal os, presents the usual arborescent appearance. The uterine walls are slightly thickened. The mucosa of the posterior wall is apparently normal. Projecting slightly from the anterior wall is a polyp (*a*) (natural size) (Cullen).

Squamous epithelioma of the body of the uterus is very rare and seen only in aged individuals in which metaplasia of the endometrium—*ichthyosis senilis uterina*—has already transformed the normal columnar epithelium into a squamous form. In cases with considerable associated keratosis distinct epithelial pearls may be found.

Adenoma of the uterus is a tumor of doubtful existence, unless it be correct to speak of the papillary hyperplasias of the endometrium seen in polypoid endometritis as adenomata, or look upon the glandular hyperplasias of the cervix as such. Such conditions are probably benign.

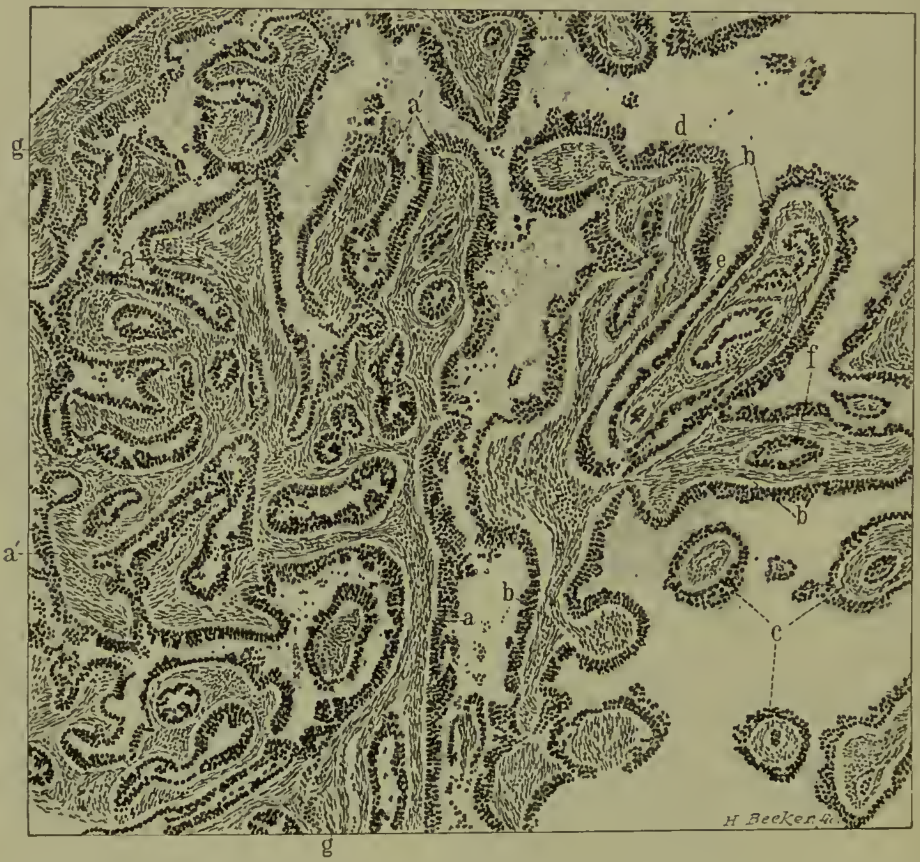

FIG. 323.—Adenocarcinoma of the cervix uteri. Almost the entire field is made up of the main trunks *a* and *b*, which send off many branches, *a'* and *b'*. *c* indicates cross-sections of terminal outgrowths. The stroma *g* consists of elongate cells with spindle-shaped nuclei. Covering the outer surfaces of the main and terminal branches are layers of epithelium, a single layer at *e*, several at *d*. (Cullen).

Adenocarcinoma, malignant or *destructive adenoma*, usually originates from the posterior wall at the fundus of the uterus. It is sessile, more or less invading the surrounding endometrium, and covered with rounded, papillary projections where not ulcerated or necrotic. The tumor consists essentially of glandular elements of quite typical appearance, which invade the subendometrial and muscular tissues. It is the muscular invasion that separates the adenocarcinoma from the non-malignant glandular outgrowths. The muscular invasion may attain such limits as to be followed by complete disintegration of the muscularis and eventual perforation of the organ. The number of glandular elements present varies, some of the papillary projections consisting solely of the tubercles and blood vessels. Many of the tubules are of the embryonal type, showing crowded, rapidly growing cells, irregularly arranged upon the limiting membrane.

The tumor grows from the tubular glands of the endometrium. Its malignancy consists chiefly in local destruction, metastasis not being common.

According to Birch-Hirschfeld, it is correct to speak of the tumor as adenocarcinoma only when, in the formation of new epithelial elements, the cells lose their relation to the membrana limitans and begin to infiltrate the tissues irregularly. Up to that time the tumor is malignant or destructive adenoma.

Carcinoma is a frequent malignant tumor which arises in the corpus of the uterus from atypical growth and development of the endometrial glands; in rare cases it develops from the cervical glands. It is a cylindric epithelioma—usually an adenocarcinoma. The tumor may be soft and disposed to rapid and extensive ulceration, or may be characterized by papillary outgrowths. The course of the tumor has already been sufficiently described in speaking of adenocarcinoma. The first metastasis is usually to the lumbar lymphatic glands.

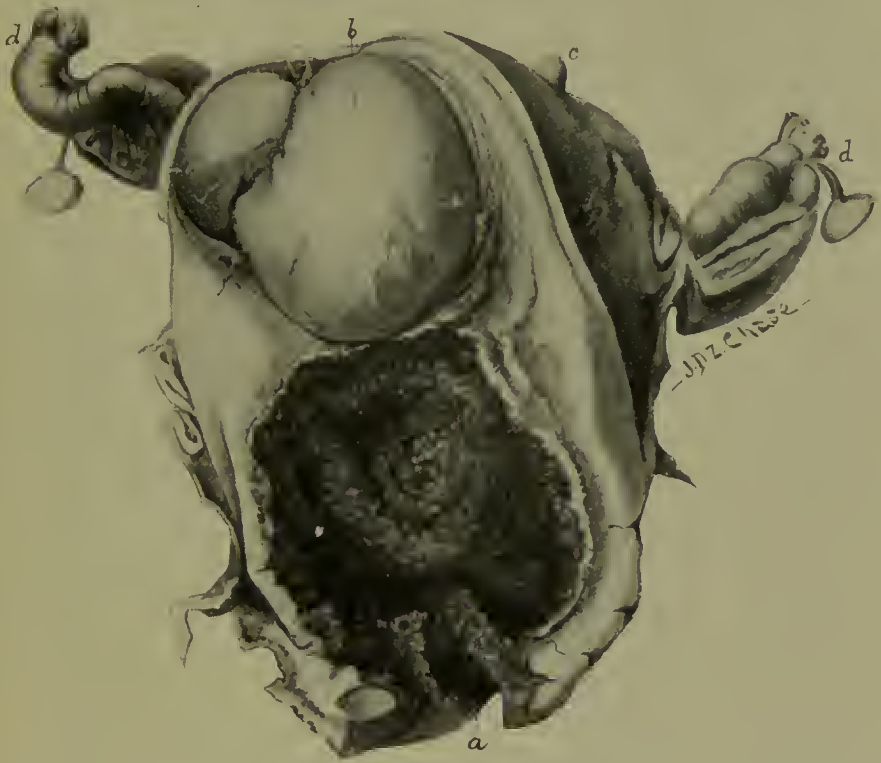

FIG. 324.—Carcinoma of the cervix uteri with interstitial fibroid tumors: *a*, Ulcerated and eroded cervix; *b*, fibroid; *c*, subperitoneal fibroid; *d*, tube, ovary, and hydatid of Morgagni.

Syncytioma malignum, or **deciduoma malignum,** also sometimes called *chorioepithelioma*, is a rare and peculiar tumor that grows at the site of placental attachment either during pregnancy or during the puerperium. It forms one or more masses of dark-colored spongy tissue, not a little like the placental tissue in appearance, and shows its malignancy by metastatic growths in the external organs of generation, in the lungs, liver, spleen, and other organs. It is usually fatal.

The histology of the tumor is very peculiar and interesting, in consequence of the embryonal tissue from which it develops and the unusual opportunities afforded by the physiologic and anatomic alterations at the time at which it occurs, for cellular growth into blood spaces. The villi of the chorion and placenta are covered with a layer known as the *syncytium*, supposed to be derived from the trophoblast of the primitive embryo.

Marchand, whose view is usually accepted, teaches that the chief cells of the tumor are derived from the *syncytium*. The cells grow in masses extending into the blood sinuses and vessels of the surrounding part of the uterus, accompanied by thrombosis in the sinuses and vessels, and a wide-spread destruction of the tissue. The growth usually shows considerable retrogressive change in the form of myxomatous degeneration and necrosis. It is almost always hemorrhagic.

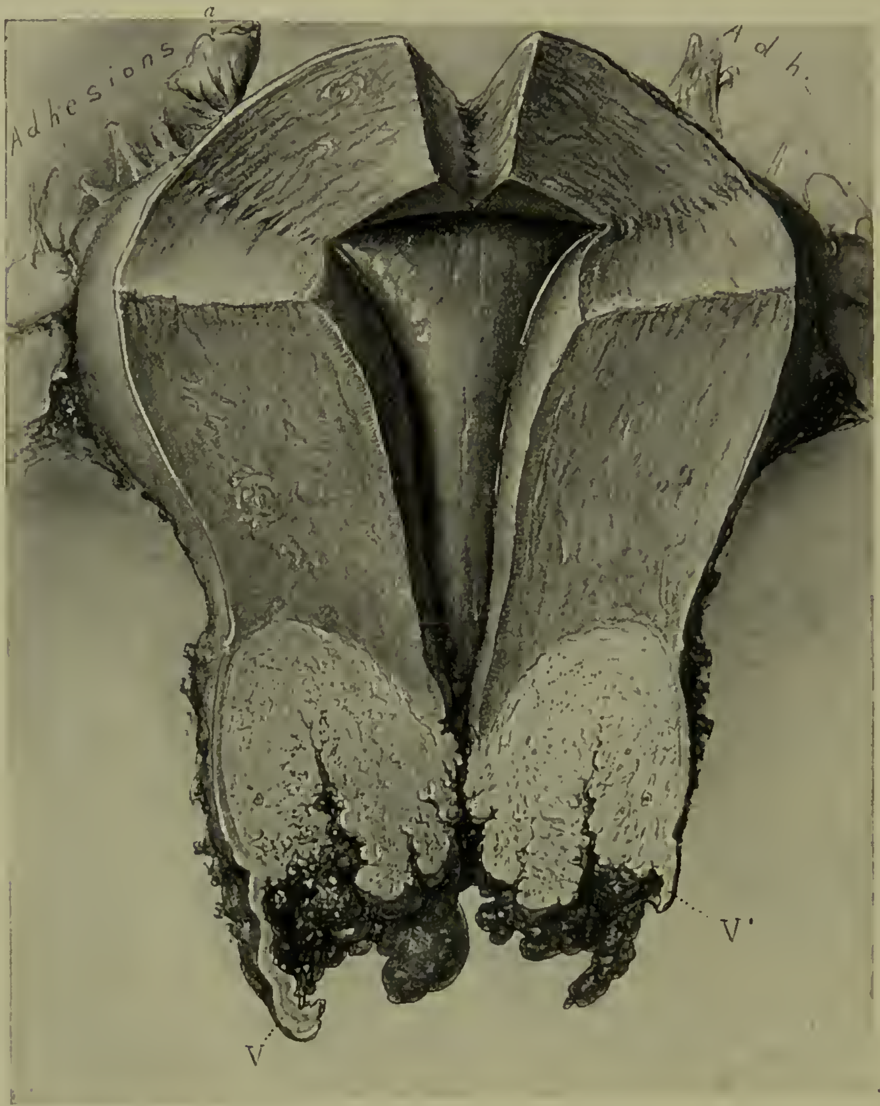

FIG. 325.—Squamous-cell carcinoma of the cervix with loss of the cervical landmarks. Attached to the outer surface of the fundus on both sides are numerous adhesions: at *a* is one of these containing adipose tissue. The entire cervix has been replaced by the new growth. The lower and ragged portion consists of large and small lobulated masses. The growth stands out in sharp contrast to the vaginal and uterine tissue, being much lighter in color. Laterally, it extends to the vaginal attachments v and v'; upward, it reaches to the internal os. The uterus is considerably enlarged, and its walls are much thickened. The mucosa appears to be normal (natural size) (Cullen).

As the cellular extension takes place into the blood sinuses, irregular masses of nucleated protoplasm are formed from the syncytial cells. In these masses large nuclei with intense staining properties are said to multiply by direct division. Other cellular masses are also present, consisting of well-differentiated cells with smaller nuclei, said to divide by karyokinesis. In these cells glycogen drops may be present. Many smaller cells resembling endothelial cells, and some still smaller, similar to lymphocytes, are also present, there being no regularity in the distribution of any of the component cellular elements. The cellular masses grow into the blood sinuses and also into the intermuscular tissue, interrupting the blood supply of the uterus and thus contributing to secondary degenerations, etc.

Cysts of the uterus sometimes occur from softening of the muscular

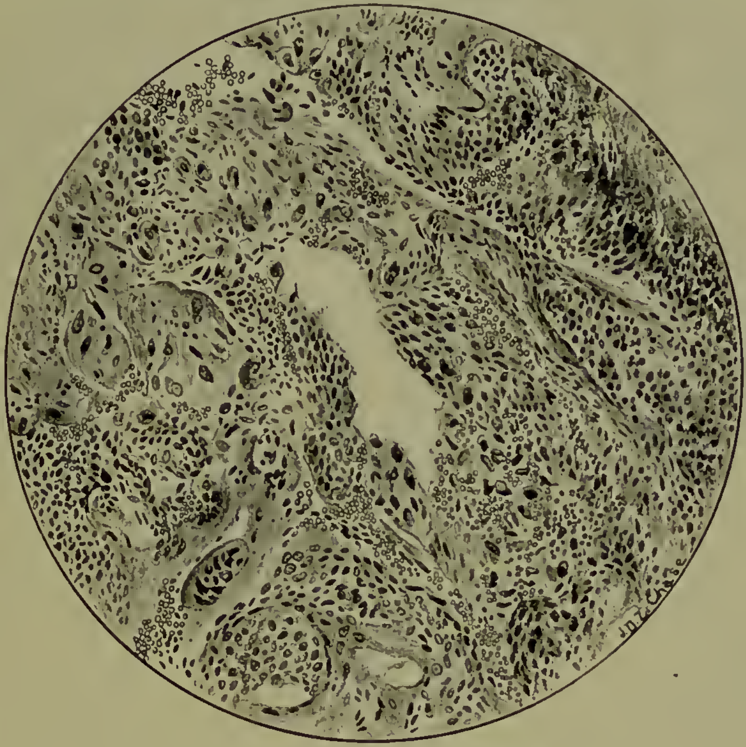

FIG. 326.—Deciduoma malignum.

tissue—*colliquation cysts.* Retention cysts occur at the cervix from obstruction of the glands—cysts or *follicles of Naboth.* Lymphangiectases also sometimes form cysts in the uterine wall. *Dermoid cysts* have been described by several writers. *Parasitic cysts,* caused by the cysticercus and echinococcus, are recorded, but are very rare. Sangalli has seen a uterus with a thickened wall occupied by numerous small serous cysts. The condition appears not to have been explained.

DISEASES OF THE VAGINA.

Prolapsus of the vagina may occur primarily—that is, independently of changes in the other organs; or it may be secondary to displacements and descents of the uterus, bladder, etc.

The primary descent of the vagina depends upon relaxation and elongation of its tissues and descent of the inferior part of the organ, either in its entire circumference or in its anterior or posterior wall, the prolapsed portion projecting between the lips of the vulva.

Cases of secondary prolapsus including the posterior wall of the bladder and carrying it into the vagina are called *rectocele vaginalis.*

Fistulous communications between the vagina and neighboring parts may result from traumatic injuries, but usually depend upon lacerations, pressure sloughs, and other injuries associated with parturition. Of these fistulæ may be mentioned the *vesicovaginal, rectovaginal, urethrovaginal,* and the *ureterovaginal.* Fistulæ sometimes also result from the rupture of abscesses, from ulcerations caused by calculi and malignant disease, and from operations.

Fistulæ vary greatly in size. They are sometimes so small as to be almost invisible, and allow only gas to enter from the rectum or an occasional drop of urine to escape from the bladder; or they may be so large that all the urine escapes through the fistula instead of the urethra, or feces constantly enter the vagina. Because of cicatricial contraction the fistulæ become smaller as they grow older unless other conditions, such as the regular entrance of urine or feces, keep them constantly stretched.

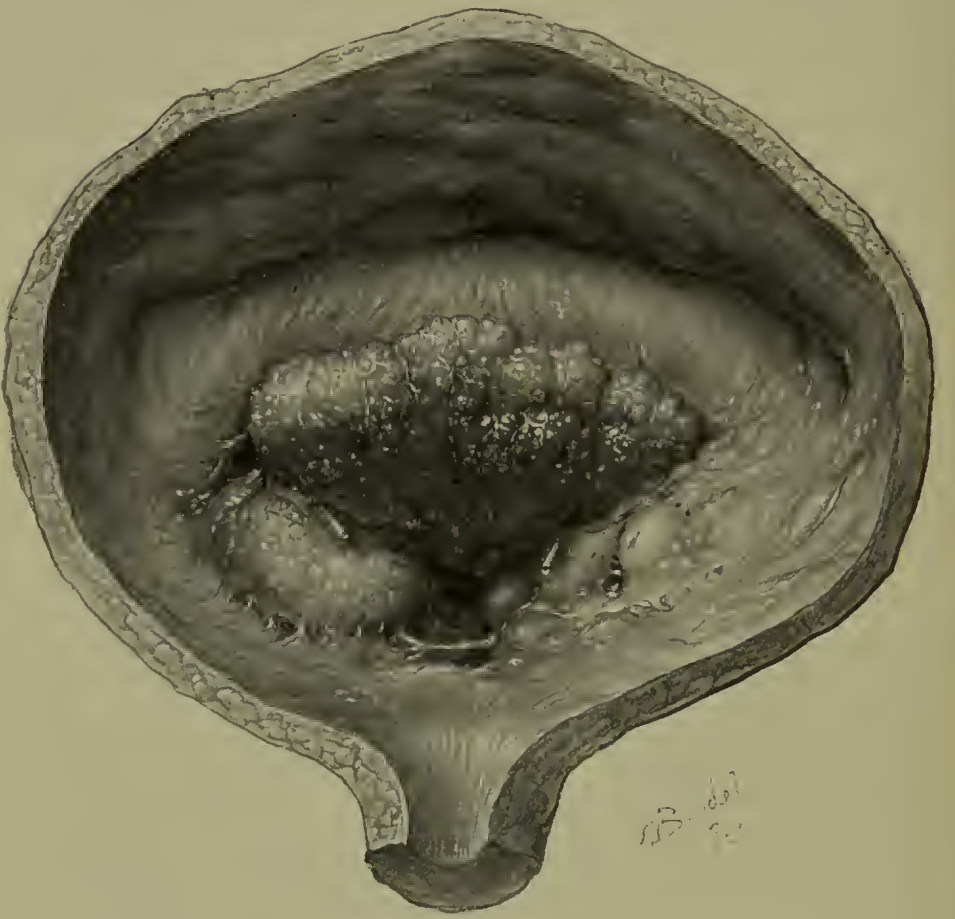

FIG. 327.—A vesicovaginal fistula seen from above, resulting from a squamous-cell carcinoma of the cervix. The inner urethral orifice is normal, but just posterior to it, and occupying the entire trigonum, is a new growth. This has elevated and clearly outlined margins, and consists of small bosses. The urethral orifices are indicated by the small catheters, and are seen opening directly on the surface of carcinomatous tissue. Just on a line with the inner urethral orifice, and almost in the center of the carcinomatous tissue, is an opening which communicates with the vagina. It has been caused by a breaking down of the carcinomatous tissue, and is a vesicovaginal fistula (natural size) (Cullen).

Traumatic injuries of the vagina are not infrequent. They may lead to inflammation, perforation, laceration, etc.; and may result in fistulæ or in cicatricial contractions and deformities which constrict or even obliterate the organ.

Colpitis, vaginitis, or inflammation of the vagina, is a frequent affection. It depends upon injuries due to coitus or to the introduction of foreign bodies, or upon the action of introduced medicaments, as carbolic and nitrate of silver, etc. It is usually caused by venereal infection, especially *gonorrhea.*

Colpitis is generally observed during adult life, but is occasionally seen in new-born infants and little girls, probably depending upon infection from the mother.

Acute catarrhal colpitis is the form usually seen. It is characterized by redness, swelling, relaxation, and exudation. The mucous membrane secretes abundant mucus, which becomes mixed with leukocytes and epithelial cells before being discharged. In gonorrheal infection the urethra and cervix uteri are usually involved.

Pseudomembranous colpitis sometimes follows the use of antiseptic douches which destroy the upper layers of epithelium and cause them to exfoliate. The exfoliation may form a true cast of the vagina.

Diphtheritic colpitis is a violent form characterized by the formation of a coherent layer of exudate upon the inflamed mucous membrane. This pseudomembrane is composed of mucus, fibrin, epithelial cells, and bacteria, the Klebs-Löffler bacillus being not infrequent in cases accompanying pharyngeal diphtheria. Pseudomembranous colpitis also occurs in other infectious diseases, such as typhoid, scarlatina, small-pox, etc. The final desquamation of the pseudomembrane is followed by erosions and ulcerations that heal later.

Dysenteric colpitis has been suggested by Eppinger as a designation for vaginitis resembling dysentery.

Phlegmonous colpitis follows the most severe forms of infection in which gangrenous inflammation and rapid tissue destruction can occur.

Gummatous colpitis (**colpitis gummosa**) is a name suggested by Winckel for a peculiar condition in which complete exfoliation of the upper layers of the vaginal mucous membrane occurs at regular periods. I have reported a case of this condition, however, in which there was no history of syphilis.

Epithelial exfoliations of the vagina also occur in consequence of astringent and caustic douches.

Chronic colpitis may succeed the acute forms, or may depend upon systemic or constitutional conditions. Birch-Hirschfeld notes that in chronic colpitis the vaginal secretions, like the normal secretions, are acid, while in acute vaginitis they are alkaline. In the chronic disease the lesions much resemble the acute catarrhal form: the mucous membrane is hyperemic, swollen, relaxed, and yields a creamy exudate. The most frequent causes of chronic vaginitis are irritation from frequent coitus and the presence of pessaries and other foreign bodies. Papillary hypertrophy of the mucosa follows prolonged vaginal irritation, and may be so excessive and wide-spread as to cause narrowing of the organ.

Mycotic colpitis is a rare result of the entrance and growth of fungi. As the vaginal secretion is normally acid, it is a good ground for the development of parasites if once a foothold is gained. Leptothrix and oidium are the most frequent parasites.

Parasitic colpitis sometimes results from the presence of a small animal parasite known as the Trichomonas vaginalis; also from the presence of the Oxyuris vermicularis.

Tuberculosis of the vagina is very rare, and usually secondary to tuberculosis of the uterus or vulva. It probably occurs in consequence of lymphatic extension, not of direct implantation from tuberculous discharges, the acid secretions protecting the vaginal tissues. It assumes the form of rounded ulcers with necrotic bases and infiltrated borders.

Syphilis of the vagina is infrequent. It usually occurs at the vulvovaginal entrance, either in the form of the chancre, the condyloma latum, or mucous patch, or as erosions following round-cell infiltrations. Gumma of the vagina may occur in tertiary syphilis, and by healing may lead to stenosis and deformity of the parts.

Tumors of the Vagina.—**Fibroma, fibromyoma,** and **myxoma** have been observed. They usually develop from the submucous and muscular layers, and project into the cavity of the vagina, covered by its mucous membrane. They may become large, and are commonly pedunculated. *Rhabdomyoma* of the vagina has been reported.

Sarcoma is rarely seen. It is usually of the spindle-cell variety, and develops from the submucous connective tissue. The tumor may remain circumscribed, or through rapid infiltration and softening may lead to extensive ulcerations.

Papilloma usually occurs as *condyloma acuminata,* and results from lack of cleanliness and from irritating discharges.

Carcinoma of the vagina is usually secondary to carcinoma of the vaginal portion of the cervix uteri. Primary carcinoma growing from the mucous glands and squamous epithelioma are rare, epithelioma being the more frequent of the two. It usually assumes a papillary form, which, when it softens, ulcerates and spreads so as to invade the bladder or rectum. Carcinoma of the vagina may be secondary to carcinoma of the rectum.

Cysts of the vagina are not common. They may be single or multiple, and are usually small, containing clear fluid, though sometimes they contain brownish or bloody fluid. The greater number are simple retention cysts of the mucous follicles. Rarer larger cysts develop from remnants of Müller's ducts or Wolff's ducts; these are characterized by the presence of columnar epithelium. Lymphangiectasis may also cause cysts.

Diseases of Bartholin's Glands.—These little glands are rarely diseased. Their ducts are sometimes obstructed by inflammation or other causes, and the secretion being retained, cystic distention occurs. In severe vaginitis they have been known to become involved and to suppurate.

Adenoma of Bartholin's glands has been reported, and it is probable that vaginal carcinoma occasionally originates from their epithelium.

DISEASES OF THE VULVA.

Traumatic lesions of the vulva are not infrequent, especially as the result of parturition. They usually take the form of lacerations, the most frequent being that of the posterior fourchet, which may extend through the perineum into the rectum. Rupture of the hymen is the usual outcome of the first coitus. In the extreme stretching to which the external genital organs are subjected during parturition, the subcutaneous and submucous vessels sometimes rupture, with the formation of interstitial hemorrhages, *hæmatoma vulvæ*, which may be as large as a man's fist or a child's head. If, through external lacerations, the mass becomes infected, gangrene may supervene, sometimes with infective thrombi in the vaginal veins, phlegmonous cellulitis, and pelvic peritonitis. More usually, however, such gangrenous changes cause puerperal infection and death.

Hyperemia of the vulva may depend upon frequent or violent coitus, onanism, the irritation of parasites, etc. *Passive hyperemia* is seen in cases of chronic venous obstruction from heart disease, etc.

Edema of the vulva chiefly affects the labia majora, causing them to swell immensely and present a vesicular appearance from the presence of serous fluid. The edema may be local, depending upon venous obstructions in the neighborhood.

Inflammation of the vulva has a variety of causes, among which may be mentioned various idiopathic and symptomatic skin diseases, parasites, abrasions from coitus and from the friction sometimes caused by walking and other movements of the limbs, uncleanness, with putrefactive changes in smegma and other discharges, gonorrhea, excoriations caused by irritating discharges from vaginal and uterine affections. In rare cases infection by the diphtheria bacillus, puerperal infection following lacerations, lesions of the specific infectious diseases, etc., may cause it.

The lesions are usually very simple, and correspond with those observed in catarrhal inflammation: redness, desquamation, excoriation, ulceration, exudation with the formation of a mucopurulent or a seropurulent discharge, rarely rapid gangrene or phlegmons, and in the diphtheritic cases, the formation of characteristic pseudomembranes.

Gangrene of the vulva sometimes occurs spontaneously in a form corresponding to the disease of the cheek called *noma*. Fortunately, this is very rare.

Tuberculosis of the vulva occurs in rare cases, usually in the form known as *lupus vulgaris*.

Syphilis.—The chancre and simple ulcerations usually occur at the borders of the nymphæ and at the orifice of the vagina. Not infrequently they are found at the commissures. The ulcerations present their characteristic parchment-like and split-pea indurations, and usually heal kindly, without marked cicatrices. Sometimes it is difficult to differentiate between the syphilitic and chancroidal ulcerations of the vulva. Mucous patches are very common upon the vulva.

Chancroid of the vulva is common, and leads to the formation of serpiginous ulcerations, and sometimes to phagedena. Inguinal buboes with suppuration usually supervene.

Elephantiasis of the vulva usually affects one or the other labium majus, though it may affect all parts of the vulva from the mons veneris to the perineum. It causes an enormous enlargement of the parts, the surface being wrinkled and nodular. Sometimes when one lip becomes greatly enlarged and pendulous, it appears like a pedunculated tumor, and, indeed, when the subcutaneous tissue of the affected part is rich in fat, it is easily mistaken for a pendulous lipoma. Elephantiasis of the clitoris may cause a penile appearance suggestive of hermaphroditism.

Tumors of the Vulva.—**Lipoma** is not infrequent, usually assuming a pendulous form. It develops from the labium majus in most cases.

Fibroma and **myofibroma** are soft, infrequent tumors. They grow from the labium majus or minus, or from the prepuce of the clitoris, and usually assume a polypoid shape, sometimes hanging as long, pedunculated bodies between the thighs.

Leiomyoma sometimes develops from the end of the round ligament.

Myxoma or **myxofibroma** is usually a fibroma with more or less mucous degeneration.

Sarcoma of the vulva is rare. It is usually a nodular tumor composed of spindle-cells.

Of the epithelial tumors, the **condyloma acuminatum,** or **venereal wart,** resulting from chronic irritation, is probably most frequent, sometimes producing such masses of papillary excrescences as to obscure the parts.

Caruncle is a papillary growth of the urethra projecting between the nymphæ and giving rise to much pain on urination.

Epithelioma of the vulva may occur in a papillary or in an ulcerating form, or as a diffuse, firm, cicatricial induration which attains considerable size before it ulcerates. The disease spreads to the vagina, urethra, and bladder, and to the skin surrounding the vulva. Softening, ulceration, putrefaction, and gangrenous changes may supervene. The disease affects the inguinal glands. Epithelioma usually originates in the clitoris or nymphæ. Carcinoma of the vulva may succeed carcinoma of Bartholin's glands.

Cysts of the vulva may depend upon retention of sebaceous matter—*atheroma*. Some are derived from hematomata. Lymphangiectasis may produce cysts. *Dermoid cysts* are occasionally seen. A rare cyst is derived from a fluid accumulation in Nuck's canal—the process of peritoneum which accompanies the round ligament of the uterus to the labium majus.

DISEASES OF THE MAMMARY GLAND.

Congenital Malformations.—It is a rare congenital anomaly to find one or both mammary glands absent, the absence of these organs seeming to be invariably associated with marked deformity of one or both sides of the chest. The nipples may be absent when the mammæ are present, or one mamma may have several nipples.

Not uncommon, on the other hand, is the occurrence of accessory mammæ, *polymastia*, which are usually situated upon the anterior aspect of the chest or abdomen below the normal glands. When present in this situation, their occurrence may be looked upon as an illustration of atavism, as most of the lower animals present numerous mammæ in pairs upon the abdomen. More rarely the accessory glands are situated upon the shoulder, upon the scapula, or upon the thigh. Supernumerary mammæ may occur in both sexes.

At birth the mammary glands are of equal size in both sexes, and about forty-eight hours afterward become enlarged and functional. From the nipple a few drops of fluid of milky appearance can be pressed, which, when examined microscopically, is found to be identical with the colostrum of preparing lactation. This secretion ceases about the seventh or tenth day, though it may continue twenty-one days and the glands remain latent until puberty, when in the female they enlarge considerably. During pregnancy, and sometimes in cases of uterine neoplasms, secretion begins and the glands enlarge.

The male glands sometimes but very rarely secrete milk (*gynecomastia*). Supernumerary as well as normal glands may be functional. After the cessation of lactation the glands diminish greatly in size and a gradual involution progresses for a long time and may almost cause the gland to disappear. After removal of the ovaries the glands gradually diminish in size, and after the menopause their glandular structure is largely replaced by fat. Obese persons sometimes have the mammæ so infiltrated with fat that the glandular tissue atrophies.

Hyperemia of the mammæ occurs in mild degree at the time of menstruation, shortly after conception, during pregnancy, and at the beginning of lactation. It is characterized by redness, swelling, and increased temperature of the parts, which are not infrequently sensitive or even painful. After death the glands when incised present a rosy appearance.

Hemorrhage is almost always the result of traumatic injuries. The blood escapes into the interstitial tissue, but may escape into the glandular tissue and be expressed from the nipple, or occasionally accumulates behind the gland, between it and the subjacent muscle. The blood may diffuse itself and be absorbed, or may collect at a single point, become encapsulated, and lead to the formation of a hematoma or blood cyst.

Hemorrhage not infrequently occurs in neoplasms.

Inflammation of the mammary gland, or **mastitis**, is occasionally of traumatic origin, resulting from bruises, etc., but in an overwhelming majority of cases it depends upon infection occurring during early lactation. It is thought by some that the infections may depend upon the entrance of pyogenic bacteria into the milk-ducts directly, and their multiplication and operation there. It has, however, been shown by experiment that the milk is sterile in many cases of mastitis until destruction of mammary tissue permits the entrance of pus into the acini or ducts.

Infection usually occurs through fissures of the nipple, and in most cases depends upon cocci that commonly frequent the skin. The chief of these are Staphylococcus pyogenes aureus and albus and Streptococcus pyogenes. These micro-organisms are brought into contact with the erected hyperemic nipple by the mouth of the sucking child. Cases of puerperal mastitis without fissured nipples are rare.

In unusual cases mastitis may depend upon inflammatory and other pathologic conditions of neighboring organs and tissues, as, for instance, caries of the ribs and erysipelas of the skin. In cases of puerperal infection, etc., the pyogenic micro-organisms may be brought to the mamma by the blood.

The course of mastitis is nearly always acute. A few cases terminate by resolution, but by far the greater number suppurate. The disease may be circumscribed or diffuse.

The **diffuse** form spreads itself over the entire gland, affecting group after group of acini, and not infrequently producing wide-spread destructive and phlegmonous lesions. It may be followed by paramastitis. This form may also become gangrenous and lead to the ultimate complete destruction of the gland.

The **circumscribed** form, which is, fortunately, much more frequent, limits its ravages to a lobe of the gland or to a group of acini, and usually terminate in a circumscribed abscess.

The mammary abscesses frequently communicate with the milk-ducts, so that the pus escapes with the milk. Sometimes the expressed secretion of the gland appears to be pure pus. At other times the abscess is more distinctly interstitial, and forms a rounded cavity full of yellowish or creamy pus, which gradually *burrows* its way to the surface of the body and evacuates. Sometimes the direction taken by the pus is downward, and after accumulating beneath the gland and dissecting it from the subjacent muscles (*paramastitis*), it perforates into the pleural cavity and terminates in empyema. Such cases may be fatal.

Mammary abscess sometimes fails to rupture altogether, the pus becoming encapsulated and subsequently calcified, remaining as hard nodes in the breast. Recovery after abscess formation occurs by cicatrization and the formation of dense scars. The external rupture of small abscesses may leave communications between the surface of the breast and the milk-ducts—*milk fistula*.

Cases of mastitis that fail to suppurate sometimes present subsequent fibrous indurations or local consolidated tissue areas in the glands.

Diffuse fibrosis of the mammary gland sometimes occurs, and is supposed to correspond to the chronic interstitial inflammation of the other glandular organs. The mamma becomes firm and hard, but is slightly, if at all, increased in size. Cystic dilatation of obstructed milk-ducts is occasionally seen. The incised gland often presents a striped appearance, depending upon alternating yellowish duct tissue and grayish-white or pink connective tissue.

Tuberculosis of the mamma is very rare as a primary affection. It is usually accompanied by wide-spread tuberculosis of other organs. The infection is probably of hematogenic origin, and subsequently distributes throughout the gland by the lymphatics and the milk-ducts. The bacilli are found inclosed in giant-cells in tubercles themselves, and, according to Verneuil and others, occur in masses in the acini of the gland, growing in the milk. This latter condition explains the occurrence of such large numbers of tubercle bacilli in the milk of tuberculous glands.

The microscopic appearance of the disease varies very much in different cases. It is usually chronic, and may be caseofibroid, leading to the formation of cheesy nodes and cicatricial bands, or it may spread more rapidly, with the formation of miliary tubercles. The glands of the cow often deceive a novice into believing that tubercles exist, where, in reality, there are none, the walls of the milk-ducts being studded with small circumscribed lymphoid collections. On the other hand, it is not infrequently true that because of their small size tubercles in the mammary gland escape observation with the naked eye.

Circumscribed local forms of mammary tuberculosis sometimes appear unexpectedly as *cold abscesses* of the breast. Superficial lesions, allied to *lupus vulgaris*, but sometimes mistaken for carcinoma, are also seen.

Syphilitic lesions of the mamma are very rare. Gumma has been seen in both hereditary and acquired syphilis. When the lesion heals, the usual dense stellate scar remains.

Hypertrophy and Hyperplasia of the Mamma.—A true hypertrophy of the mamma is sometimes seen in the period of glandular proliferation that takes place at puberty. Instead of ceasing at the normal size, the breasts continue to increase until they become enormous and pendulous, weighing many pounds, and sometimes reaching to the pubis. Subsequent involution is rare. Both breasts are affected, though one is usually larger than the other. When persons so afflicted become pregnant and subsequently lactate, the milk is secreted in enormous quantities (*galactorrhea*). The cause of the hypertrophy is unknown.

Enlargement of the mammary glands also sometimes depends upon diffuse fatty infiltration (*lipomatosis*).

Elephantiasis of the mammæ produces a diffuse hyperplasia of the areolar tissue, enormously enlarging the size of the glands. The skin covering the organs in elephantiasis is velvety in appearance.

Tumors of the Mammary Gland.—Connective-tissue tumors of the mamma are less frequent than those of glandular type. They form rounded, circumscribed, encapsulated growths, usually single, which arise from the interstitial tissue, press the glandular tissue aside, and rarely attain a large size.

Fibroma, myxofibroma, myxoma, and **lipoma** occur, but are infrequent. One case of *leiomyoma* of the nipple is on record. Cartilage, striped muscle-fibers, and bone have been found in mixed tumors of the breast.

Sarcoma is a frequent tumor, and usually of the round-cell form, though spindle-cell sarcoma is also observed. Rarely combinations of round- and spindle-cells occur. Sarcoma may be diffuse or circumscribed, but, except in diffuse large round-cell sarcoma, which may be mistaken microscopically for carcinoma, their recognition is easy.

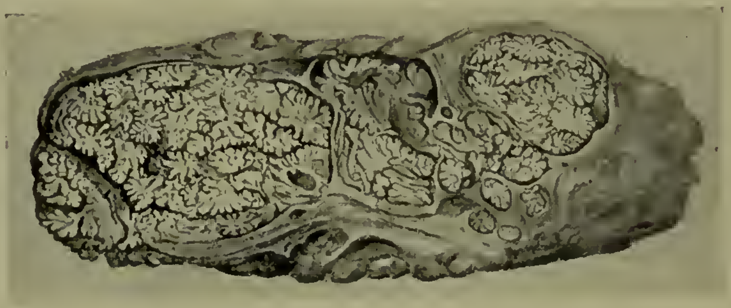

FIG. 328.—Cystic fibroma of the breast (Warren).

Circumscribed spindle-cell mammary sarcoma sometimes presents an interesting radiating appearance to the naked eye.

Fibrosarcoma is not uncommon, and telangiectasis and cystic conditions frequently occur.

Giant-cell sarcoma, *alveolar sarcoma*, and *pigmented sarcoma*, sometimes occur. These are all circumscribed tumors, rounded in shape, and often lobulated.

The *diffuse mammary sarcoma* may be confused with hypertrophy of the mamma. It is, however, usually unilateral, infiltrates in all directions, soon extending to the skin, which then becomes immovably fixed upon the tumor. Cyst formation is common both from obstruction of the milk-ducts, by which smooth-walled cysts are formed, and from degeneration of the tumor tissue. To tumors of this kind Virchow applied the name *cystosarcoma*. Sometimes the sarcoma tissue grows into the cysts, compressing them and subsequently filling their cavities, thus producing an *intracanalicular sarcoma* or *sarcoma phylloides*, as Müller has called it.

Sarcomata may grow from any part of the connective tissue of the mammary gland, though probably most frequently from that near the milk-ducts and nipple. Sometimes glandular ducts and acini are caught and incorporated in the growth, giving the tumor the appearance of consisting of both embryonal connective tissue and epithelial acini.

The sarcoma is, in general, malignant, though the degree of malignancy is modified by its diffuse or encapsulated condition, its vascularity, etc. It is, however, far less malignant in every way than the carcinoma, and metastasis is not so common.

Adenoma is one of the most frequent tumors of the mammary gland. It is very varied in appearance, and the term adenoma is now applied to all tumors of the mammary gland not carcinomata, in which glandular tissue forms an important element.

Pure adenoma composed of glandular acini and ducts bound together by a small amount of connective tissue, and inclosed in a distinct capsule, seems to be a rare tumor, of which I have seen but one specimen.

The great majority of the tumors are combined with such a large amount of fibrous tissue as to make it necessary to use such terms as *adenofibroma* and *fibroadenoma* for their proper description. Nearly all the tumors contain both ducts and acini, though the proportion is not normal, and it becomes necessary to speak of *canalicular* or *tubular* and *alveolar* or *racemose* varieties.

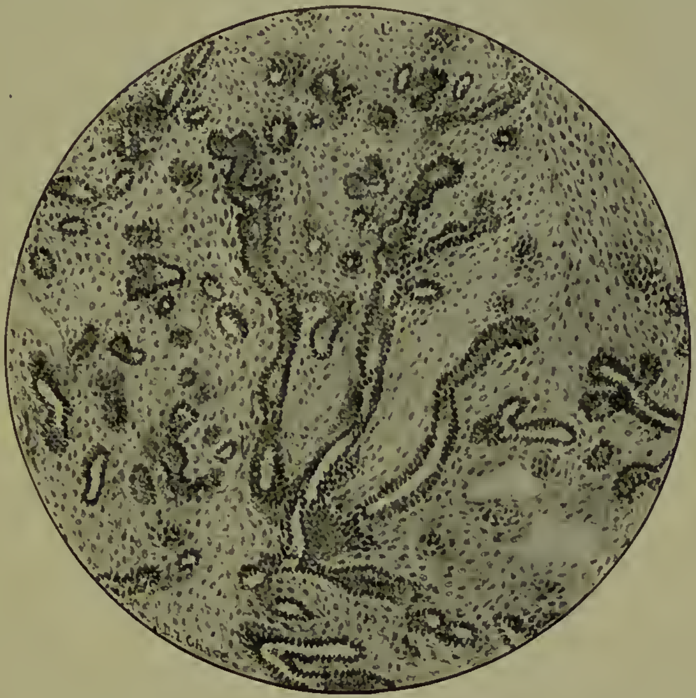

FIG. 329.—Fibroadenoma of the mammary gland (canalicular form) (Oc. 2; Ob. 3).

The fibroadenoma is sometimes distinctly circumscribed by connective tissue. Such a capsule is, however, more likely to be intimately connected with the tissue of the breast and tumor than in the other benign tumors.

The tumors probably never spring from their nidus when the capsule is incised. Sometimes the growth is only partly encapsulated, sometimes not at all.

The relation of the connective tissue to the glandular elements is of interest, and makes easy three divisions of these tumors :

Intercanalicular adenoma, in which the tumor is chiefly fibrous in structure, with the ducts and acini irregularly distributed through it.

Pericanalicular adenoma, in which the fibrous tissue makes distinct concentric investments of the ducts and groups of acini.

Intracanalicular adenoma, in which polypoid or papillary growths extend into the ducts.

The question of encapsulation probably has a direct bearing upon the malignancy of the tumor, and tumors removed by the surgeon and sent to a laboratory for diagnosis should be carefully inquired into. Incomplete encapsulation is often spoken of by the surgeon as *adherent capsule*, and is to be looked upon as an indication that the separation of the tumor from the mammary gland itself is not complete, so that any change taking place within the tumor may readily extend to the gland. It is also possible that many of the incompletely encapsulated tumors arise from the breast tissue itself, being little more than hyperplastic lobules surrounded by connective tissue that has been pushed aside in their growth. In other cases they are incipient carcinomata. The completely encapsulated tumors may, at times, be the result of the inclusion, and later development, of fetal elements, and in them are sometimes unexpectedly found fragments of adipose, chondrous, muscular, or even osseous tissue (*sequestration dermoid tumors*).

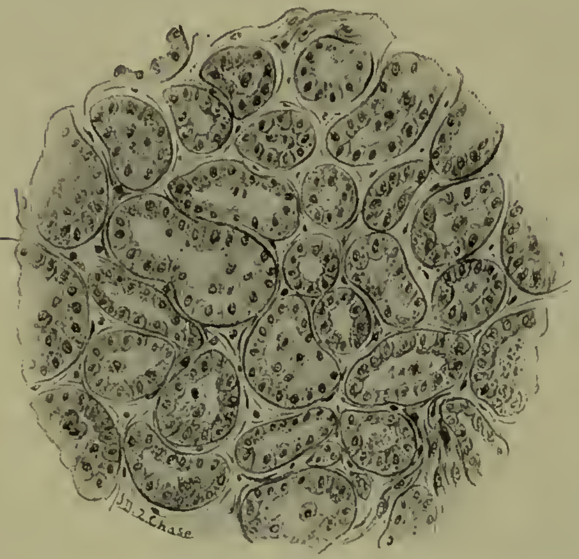

FIG. 330.—Alveolar adenoma of the mammary gland (Oc. 2; Ob. 9).

Cystic adenoma or *adenocystoma* is an adenoma in which cysts are formed. They are nearly always retention cysts, formed by the accumulation of the glandular secretion in cecal ducts, though they rarely result from hemorrhagic extravasations or from softening of the tissues. The cysts usually have smooth walls, and vary in size from a pin-head to a goose-egg. They contain seromucus, more rarely milky fluid. Sometimes they contain masses of epithelial cells of horny nature. The formation of the cysts usually takes place in the already formed tumor. Some observers are of the opinion that the tumors develop about cysts formed from preëxistent mammary ducts.

Within the smooth-walled cysts papillary outgrowths commonly develop, so that the adenocystoma becomes *adenocystoma papilliferum*. The papillary growths may occur in very small cysts or in the large ones only. They bear no definite relationship to the magnitude of the cyst, which may be completely filled with their cauliflower-like excrescences, or may contain a few very small villous outgrowths. Large cysts may contain immense masses of papillæ, filling and even distending them. Only a few of the cysts may show the papilliferous change, or every cyst may be full of them, so that the tumor, which really contains cysts of every size up to that of a hen's egg, may apparently be of solid consistence. In addition to the papillæ the cysts usually contain a small amount of clouded fluid.

The intracystic growths are checked in development by the resistance of the surrounding tissues, but it sometimes happens, when the cysts are large and superficially situated, that the pressure which they exert upon the suprajacent skin and fascia causes them to attenuate gradually and ultimately to ulcerate, rupture, and permit the intracystic growth to project upon the surface of the skin with an appearance closely resembling fungous granulations. The projecting masses are red and vascular, soft and tender, and continue to increase in size and form larger and larger openings through which to project.

The papillæ that develop within the cyst are covered with a single layer of columnar epithelium and consist of delicate, vascularized, sometimes myxomatous tissue. Sometimes the epithelial lining of the cysts and covering of the papillæ take on a remarkably active development, extending in columns from the papillæ to the cyst-wall, forming numerous layers upon the mucous membrane and even filling up the intracystic spaces.

Concerning the histology of the mammary adenomata very little more need be said. In general they closely resemble the structure of the gland in

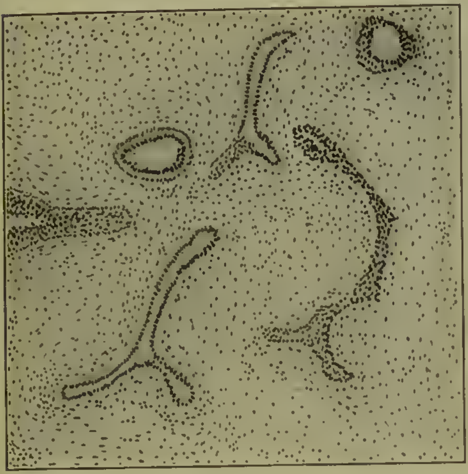

Fig. 331.

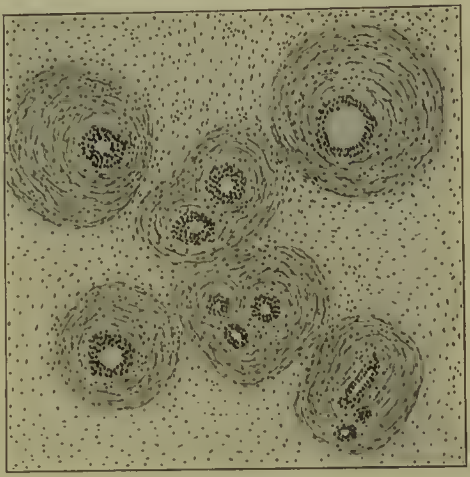

Fig. 332.

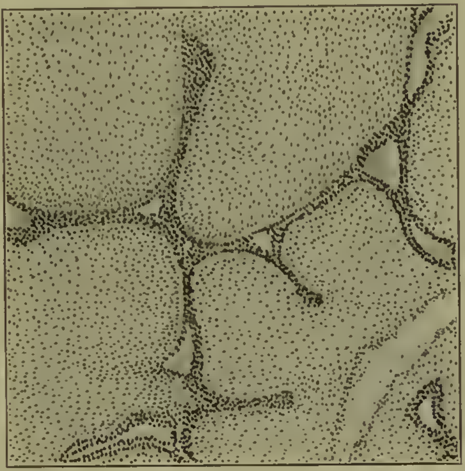

Fig. 333.

FIG. 331.—Intercanalicular adenofibroma of mamma. The fibroconnective tissue bears no definite relation to the glandular canals.

FIG. 332.—Pericanalicular adenofibroma of mamma. The fibroconnective tissue shows a peculiar concentric relation to the glandular canals.

FIG. 333.—Intracanalicular adenofibroma of mamma. Papillary connective-tissue growths project into the glandular canals.

the character of their cellular elements and the size, appearance, and arrangement of the cells. The large cysts of the adenocystoma usually have a cuboidal or columnar epithelium originating from the ducts, not from the acini, and the papilliferous cysts have epithelial cells of the same kind.

Adenomata usually develop early in life—that is, before the thirty-fifth or fortieth year. They not infrequently seem to begin their growth at puberty, remaining unnoticed until of considerable size. A few cases have been observed in which the tumors have spontaneously become reduced in size—possibly by absorption of the contents of the cysts.

In general it may be said that the adenoma is benign. There is, however, no sharp line separating the adenoma from the carcinoma, especially in the forms not well encapsulated, and in the papilliferous forms; and unless the tumor be carefully studied in various parts and the possibility of its connection with the breast tissue considered, the prognosis should always be given with reserve.

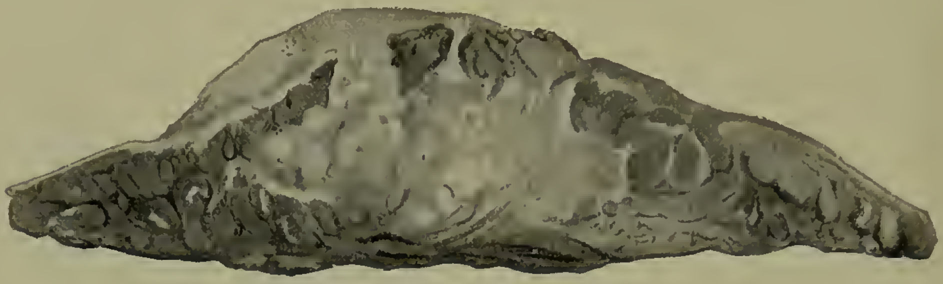

FIG. 334.—Carcinoma of the breast; extension of the disease to the surface through the ligaments of Sir Astley Cooper (Warren).

The papilliferous form is chiefly destructive by its local effects. All that give lymphatic metastasis should be considered *carcinoma* irrespective of the histologically typical appearances of parts of the tumor.

Carcinoma of the mammary gland is probably the most frequent malignant tumor, and is certainly the most frequent malignant tumor of the mammary gland. It affects both men and women, but is very rare in the former, occurring in only 2 per cent. of the cases studied by Paget. The usual period of its development is between the thirtieth and sixtieth years of life, though it sometimes occurs earlier and later. The great majority of cases occur between the fortieth and fiftieth years.

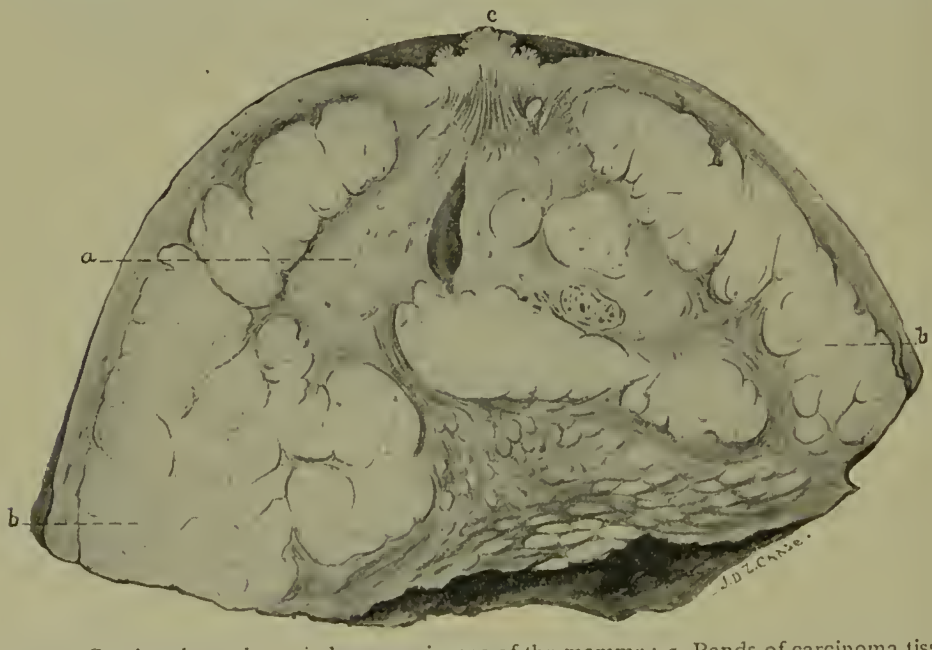

FIG. 335.—Section through a scirrhous carcinoma of the mamma: *a*, Bands of carcinoma tissue consisting chiefly of connective tissue with cell-nests; *b*, fatty tissue; *c*, retracted nipple.

The tumor is usually unilateral and affects the right breast a little more frequently than the left. It is not uncommon for both breasts to be simultaneously affected, and in rare cases carcinoma of both breasts has been known to occur in association with primary independent tumors of the internal organs.

The tumor is one of the most malignant, and is usually fatal. Its course from inception to fatality is of varied duration according to the particular variety of the growth and the peculiarities of the individual. It is not known what circumstances modify these conditions. The growth may be fatal within six months or may be present without very marked progress for twenty-five years or more.

The greater number of mammary cancers arise from atypical growths of the epithelium of some local lobule of the gland, so that they present themselves in the form of irregular, more or less well-circumscribed nodules which are no doubt often mistaken for adenomata with *adherent* capsules. More rarely the growth seems to affect the gland to a considerable extent simultaneously, causing the formation of an indefinite induration which is not movable within the gland and becomes adherent to the suprajacent skin.

The skin above the tumor nearly always presents a peculiar white color, and being smooth and coarse, is sometimes described as *pig-skin*. The nipple is retracted.

Carcinoma develops at times from the acinose tissue, and maintains pretty well a racemose type, so that it seems correct to differentiate between *alveolar carcinoma* and *tubular* or *duct carcinoma*, in which the cells, instead of occurring in small irregular nests, form long tubular or cylindric aggregations. Sometimes the cells have a distinctly columnar or cuboidal tendency, suggesting origin from the ducts rather than from the acini. The ordinary mammary carcinoma is usually spoken of as *carcinoma simplex*.

The tumor sometimes grows rapidly, attains a large size, and is soft and juicy. In such cases histologic examination shows large cell-nests with little intermediate connective tissue, and such tumors are usually termed *encephaloid* or *soft*, to distinguish them from the *scirrhous* or *hard* forms, in which the connective tissue is cicatricial in character, considerable in amount, and contains comparatively few irregular cell-nests of small size. The connective tissue in carcinoma, especially in the scirrhous form, produces the characteristic *retraction of the nipple* by contraction.

The destructive effects of mammary carcinoma are illustrated by the disorganization of the gland, the occurrence of areas of malnutrition, with the formation of cysts by softening, the obstruction of ducts and formation of retention cysts, the extension of the disease to the skin, and the occurrence of ulcerations, and by early metastasis to the axillary, subclavicular, and supraclavicular lymphatic glands, and later to the internal viscera.

Colloid carcinoma of the mamma is rare, and in tumors so denominated, instead of an actual colloid degeneration of the epithelial cells, mucoid degeneration of the interstitial tissue gives the gelatinous consistence.

Calcareous infiltration not infrequently occurs in the dense stroma of the organ, in the inspissated contents of cysts, etc. Rarely concentric mineral bodies occur in the cell-nests. The epithelial cells of the tumor are sometimes so pressed upon by the surrounding fibroconnective tissue that they undergo atrophy from fatty change. The constriction of blood vessels by the connective tissue also causes local malnutrition and ultimate fatty degeneration of the epithelium and mucous degeneration of the stroma. While the retrogressive changes are occurring in the older parts of the tumor, a rapid multiplication of the young healthy cells of the periphery is usually invading new territory and the disease is advancing steadily.

Cases of spontaneous recovery from carcinoma are extremely rare, and surgical eradication not infrequently fails to interrupt the disease because of the early and wide-spread lymphatic metastases.

Paget's disease of the nipple is a peculiar carcinomatous affection of the skin covering the nipple and areola. The disease usually occurs in very aged women and may remain local for years. In general characteristics it resembles chronic eczema, with which it was, in fact, confounded until Paget showed its true nature and its not infrequent disposition to descend into the mamma with resulting true carcinoma. In advanced cases the nipple may be so completely destroyed as to be absent both on microscopic and on macroscopic examination. The *psorosperms*, which are said to occur in the cells in this affection, and which were regarded by Darier as *sporozoa*, are of very questionable parasitic nature, the present tendency being to look upon them as diseased *prickle-cells* of the skin.

Cysts of the mammary gland are not infrequent. The most frequent are observed in such morbid growths as cystoma. Independent retention cysts or *galactoceles* are sometimes observed. They occur during the involution of the gland following lactation, and are sometimes called *involution cysts*. They are usually the size of a pea, and may be numerous. Cysts occur in carcinoma and sarcoma, sometimes from retention of secretion, sometimes from interstitial hemorrhages, sometimes from the softening of neoplasms.

Parasites of the mammary gland are very rare. The *Tænia echinococcus* has been encountered in about sixteen cases. The *Cysticercus cellulosæ* has also been seen a few times.

CHAPTER X.

THE URINARY SYSTEM.

THE KIDNEY.

Congenital Malformations.—In rare cases of marked congenital malformation the kidneys may be absent, and the individual unfitted for postnatal existence. Congenital absence of one kidney is occasionally seen in otherwise normal individuals, the absent organ usually being that of the left side. In such cases the existing organ is considerably larger than normal.

More frequent than total absence of the kidney is a congenital atrophy by which the kidney is represented by a connective-tissue rudiment a few centimeters long, very thin and narrow, and almost entirely without glandular substance. The atrophic condition may result from diminished blood supply or failure of the Wolffian body properly to transform itself; from inflammatory conditions, and from irregularities of growth and development not very well understood.

The most frequent congenital variations from the normal are a peculiar lobulation, consisting of retention of the fetal lobules with marked sulci between them; union of the two organs into one large *horse-shoe* kidney; multiple cysts, and double ureters.

Horse-shoe kidneys are formed by the fusion of the lower, or in less frequent cases the upper, inner surfaces; rarely, the entire median aspects of the organs. The condition is naturally accompanied by more or less displacement of the organs, which are unusually approximated and situated lower in the abdomen than normal.. Horse-shoe kidneys have an anterior central hilum, with one or two pelves and from two to four ureters. The ureters may be abnormally short if the organ be very low and near the bladder. The blood vessels of these kidneys are almost always anomalous, and very frequently more numerous than normal. It is supposed that the horse-shoe kidney depends upon abnormal proximity of the developing organs, with subsequent fission.

Occasionally one or the other kidney is abnormally attached to the surrounding parts, the left organ then descending toward the sacrum and approaching the median line, its vessels having an anomalous origin and the ureter being very short, the right kidney freely movable, with a normal vascular supply and ureter. The abnormality thus consists in a remarkable degree of relaxation of the peritoneal covering of the organ, permitting it to prolapse and hang in a pendulous fashion in the lower part of the abdomen or even to enter the pelvis. Such an organ is described as a *floating kidney*, and can be pushed about from place to place in the abdominal cavity. It is sometimes mistaken for an abdominal tumor.

Double ureters usually result from congenital division of the urinary tract. They may be double throughout their entire length, or only partly so, depending upon their origin from early or late division of the urinary tract. Double ureters may end normally in the bladder, but in rare cases they enter the seminal vesicles, urethra, uterus, or vagina.

Not infrequently cases are observed in which the ureters are obstructed by kinks or folds of mucous membrane, so that they become enormously dilated. The dilatation of the ureter is succeeded by dilatation of the pelvis of the kidney, and later by dilatation of the kidney itself, the parenchymatous tissue of which yields to the pressure of the accumulating urine as long as secretion is possible, eventually becoming transformed into a sac with the external appearances of a kidney, but with its substance reduced to a thin rind a few centimeters in thickness, composed chiefly of fibrous tissue inclosing a few tubules and glomerules, and surrounding the accumulated fluid. Such an appearance is described as *hydronephrosis*.

Disturbances of the Renal Circulation.—**Anemia** in the kidney may result from the gradual obstruction of the arteries by the pressure of diseased organs and morbid growths; from obstructive endarteritis or from diseases accompanied by arterial contraction, such as lead-poisoning, epilepsy, tetanus, etc.

The affected organ is small, bloodless, pale, and may show signs of necrosis. If the change occur only in limited areas of the organ, it will appear mottled, with pale-colored patches.

The anemic organ, receiving little blood from which to secrete urine, is in consequence practically thrown out of service, though its power is probably not suspended as long as its vitality persists. Profound anemia of the kidneys is accompanied by alteration of secretion, the urine under such circumstances becoming albuminous.

Renal anemia is serious only when persistent. In transitory cases, the circulation being reëstablished, the normal condition soon returns. In persistent cases atrophy follows. Degeneration usually begins in the glomerules, but soon embraces the parenchyma. Fatty metamorphosis is the usual form of degeneration. Actual necrosis may occur.

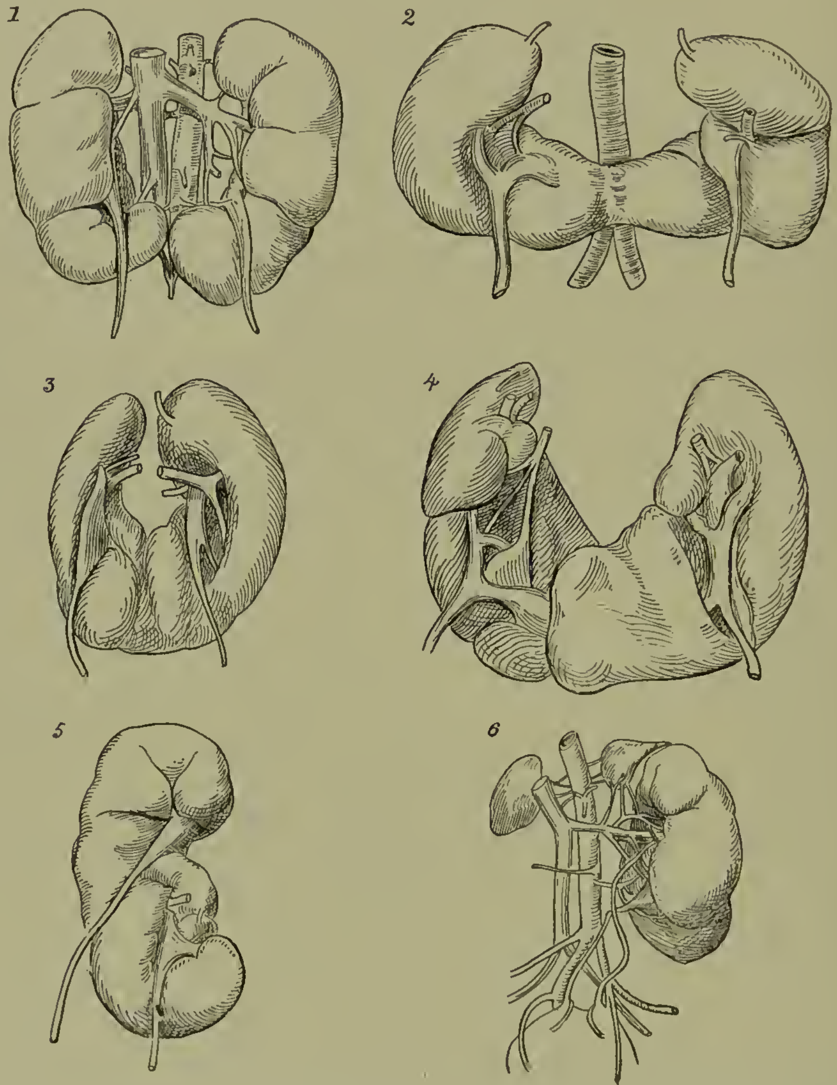

FIG. 336.—Diagrammatic representation of the congenital malformations of the kidney (fused kidneys): 1, Partial fusion of the organs at the inferior extremities; 2, common form of "horse-shoe kidney"; 3, 4, marked fusion of inferior internal surfaces; 5, sigmoid kidney; 6, double kidney (modified from Newmann).

Acute hyperemia of the kidney may be toxic, infectious, nervous, or collateral.

In various *intoxications* the elimination of the poison by the kidneys is accompanied by more or less injury, of which hyperemia is the first expression. This is seen in poisoning by ether, chloroform, cantharides, turpentine, numerous drugs and bacterial toxins, and possibly by certain of the leukomains.

In *infectious diseases* the toxins that reach the kidney in the blood, as well as those produced by bacteria colonized in the organ, may similarly occasion hyperemia.

Hyperemias of *nervous origin* are for the most part physiologic and occur in response to reflex stimulation. Exaggerations of the condition may be pathologic.

Collateral hyperemia occurs in consequence of sclerosis of the aorta and larger blood vessels, with loss of the elasticity normally compensating for the cardiac impacts. When this elasticity is lost, the pulsations of the heart result in an increased arterial pressure and persistent hyperemia of the kidney, with resulting polyuria and structural changes.

Morbid Anatomy.—In active hyperemia the kidney is slightly enlarged, soft but elastic, reddish in color, and its substance moist. Upon section, considerable blood escapes. The congestion is diffuse, not localized in the bases of the pyramids.

Upon microscopic examination the glomerules and intertubular capillaries are found turgescent, the interstitial tissue slightly edematous, the secreting cells clouded and sometimes degenerated, it being impossible to draw any sharp line between the point at which congestion ends and degeneration begins. In reality it seems as if the congestion simply accompanied the degeneration, the two depending upon the same cause.

In persistent collateral hyperemia the effect of the increased blood-pressure, together with the occurrence of some sclerotic changes in the vessels, results in rupture and occlusion of capillaries with loss of glomerules and atrophic changes in the organ similar if not identical with those observed in arteriosclerosis (*q. v.*).

Morbid Physiology.—Hyperemic kidneys secrete urine which may contain some red blood corpuscles, a trace of albumin and soft cylindric bodies, resembling tube-casts, known as *cylindroids*.

Passive Hyperemia of the Kidney (Cyanotic Induration).—This is a very common and important accompaniment of those conditions in which the venous blood-pressure is elevated. It occurs in valvular heart disease, in chronic disease of the lungs, in thrombosis and other obstructions of the vena cava, and also results from the pressure of morbid growths upon the veins of the kidney.

Morbid Anatomy.—In the *rare acute cases* resulting from venous thrombosis, etc., the vessels of the organ become suddenly distended with venous blood. The kidney is then larger than normal, dark in color, and soft in consistence. The capsule strips off readily, the cut surface drips with blood, and on the surface of the section the bleeding cut veins can be seen. Subcapsular hemorrhagic spots are also present. The chief congestion occurs about the bases of the pyramids, but the entire organ may be filled with blood.

When examined microscopically, the important changes consist in turgescence of the vessels and numerous extravasations of blood into the capsules of Bowman and into the tubules.

The *chronic cases* are rather less marked, for the length of time during which the condition has persisted makes possible the establishment of numerous collateral venous trunks by which the blood finds a more ready exit. The organ is enlarged and usually somewhat edematous. There are no subcapsular hemorrhages. The capsule strips less readily than in the acute cases, the cut surface, while moist with blood, bleeds less than in the other form, and dilated veins are not conspicuous. The appearances, both macroscopic and microscopic, will be modified by the duration of the lesion and the degree of venous obstruction present. In ordinary cases depending upon cardiac lesions, as time goes on, the kidney becomes more and more changed to accommodate itself to the congestion, this change consisting largely in hyperplasia of the intertubular connective tissue, by which greater support is afforded to the distended veins. The vessels are dilated and gape when cut; their walls are thick. The organ in this *indurated stage* appears a little larger than normal, is dark and *cyanotic*, or pale if much connective-tissue contraction has occurred. To the touch it is distinctly indurated. The surface is likely to be roughened and pitted from newly formed bands of connective tissue within the organ, which draw upon the capsule. If the induration be marked, the capsule does not strip off readily.

Microscopically can be noted the increase of connective tissue. Some of the epithelial cells of the tubules are fatty degenerated or atrophic, especially in the straight tubes of the medullary substance. Here and there a glomerule is seen to be destroyed—transformed into homogeneous or slightly granular detritus—but the greater number of glomerules are normal. Tubules connected with the destroyed glomerules are found to be atrophic. Hyaline tube-casts occur in some of the tubules. Brownish pigment-granules resulting from hemolysis, and sometimes crystalline pigment, occur in the epithelial cells and in the tubules.

Morbid Physiology.—In chronic passive congestion of the kidney the quantity of urine secreted is diminished. It contains a larger or smaller number of red and white blood corpuscles, some albumin, and few hyaline tube-casts.

When, from either active or passive hyperemia or because of disease of the vessels of the kidney, the blood-pressure in the capillaries becomes greater than can be borne, *hemorrhages* occur.

These hemorrhages are usually minute, and may be interstitial or intratubular. In the former case the intertubular capillaries rupture and the blood escapes into the interstices of the tissue, where its collections, irregular in size and extending along the tubules, can plainly be seen with the microscope. These little collections of blood are soon removed by natural processes.

When the hemorrhage is intratubular, it probably depends upon the rupture of capillaries in the glomerule and the escape of blood into Bowman's capsule. The blood, when in very small amounts, flows down the tubule, and the blood corpuscles are found isolated and comparatively unchanged in the urine. When in more considerable amounts, it fills the tubules, coagulates within them, and appears in microscopic sections as yellowish streaks. The coagula sometimes escape entire into the urine, constituting what are known as *blood-casts*. When retained, the coagulum is slowly absorbed, the hemoglobin of the corpuscles being dissolved out and finding its way, probably in a changed form, into the epithelial cells of the tubule, where it appears as a yellowish droplet.

Intratubular hemorrhages can also occur from rupture of the tubules in interstitial hemorrhage.

Collections of pigment in the kidney resulting from any cause are sometimes described as *pigment infarcts*.

In cases of active hemolysis with rapid elimination of hemoglobin through the kidney it is common to have the hemoglobin accumulate in drops in the epithelial cells of the tubules. Crystals of hemoglobin may also collect in the tubules—*hemoglobin infarcts*.

The modified pigment known as *bilirubin*, when present in excess in the blood plasma, is also excreted by the kidney, and appears as larger or smaller granules in the epithelial cells of the uriniferous tubules. Crystals are rarely seen, except in *icterus neonatorum*. The pigment accumulations of the kidney occur more frequently in the cortical substance in adults and in the medullary substance in infants.

Arteriosclerosis of the Kidney.—The blood vessels of the organ not being all and equally affected, the interesting changes characteristic of the process are not equally distributed, and the kidney becomes irregularly affected, presenting a varied appearance.

Etiology.—Senility, gout, lead-poisoning, alcoholism, and syphilis are the most frequent causes.

Morbid Anatomy.—The gradual occlusion of the vessels caused by the obstruction is responsible for the changes in the organ. When the obstruction of a small vessel is sufficient to incapacitate it from nourishing the tissue which it supplies, atrophy of that part of the parenchyma follows. The first change is observed in the glomerule, which, losing its normal mulberry appearance by the disappearance of the nuclei of its cells and by its imperviousness to the passage of blood through its capillary tubes, becomes transformed into a homogeneous or slightly granular mass. If the sclerotic process involves a very small vessel, only one glomerule may show the change; but if an interlobular artery be affected, all the glomerules in its distribution will be altered.

Because of the imperviousness of the glomerule the blood of the afferent vessel empties directly into the efferent vessel, and in cases in which many glomerules are destroyed, the blood seeks an entirely new course, by which, instead of passing through the intertubular capillary network, it enters the larger veins from the widely dilated *arteriolæ rectæ* of the medullary substance.

The suspension of glomerular function seems to be invariably followed by atrophy of the consequently useless uriniferous tubule, to which it supplied water, and in microscopic specimens these elements can be found much contracted, the cells reduced in bulk, their striations and individual peculiarities lost, and the whole tubule reduced to the size of Henle's loop, or sometimes even to that of a blood capillary. The remaining functional glomerules appear to be increased in size. The loss of kidney substance resulting from the local atrophic changes causes the formation of depressions upon the surface of the organ corresponding to the lost tissue. The external appearance of the organ thus becomes quite characteristic.

In general it may be said that the arteriosclerotic kidney is smaller than normal, firm from loss of parenchymatous elements and from retention of the fibrous elements. Its external surface is marked by pits and sulci corresponding to the atrophic areas. It may be possible, with the naked eye, to observe sclerotic changes in the larger vessels, and at the medullary part of the organ vessels that should be small and inconspicuous appear prominent, dilated, and stiff. The capsule can be removed without much difficulty, but the exposed surface is granular, pitted, and fissured.

Pathologic Histology.—Microscopically the changes in the blood vessels are usually evident. Both destroyed and hypertrophied glomerules are conspicuous, as are also the atrophied tubules. In uncomplicated cases of arteriosclerosis the connective tissue of the organ is probably not really increased, though it seems to be because of the loss of parenchyma.

Many of the tufts are surrounded by greatly thickened capsules, the significance of which is not clear. These capsules contract upon the destroyed glomerules, reducing them to smaller and smaller size until they are represented by small fibrous nodes.

Remembering that the causes which lead to arteriosclerosis also bring about chronic interstitial nephritis, it is unwise to attribute all the changes observed in the arteriosclerotic kidney to the alterations of circulation. Some of them, and especially any real increase in the connective tissue present, may depend upon chronic inflammation of the organ.

It is very common to find collections of lymphocytes in the atrophic arteriosclerotic areas. Their significance is not understood.

Pathologic Physiology.—The loss of glomerules and the atrophy of the associated tubules necessarily diminish the secretory power of the kidney. As, however, what remains of the kidney structure is comparatively normal, it is able to maintain its function almost indefinitely. It becomes, therefore, a condition that contributes toward, rather than occasions, serious trouble to the patient.

Infarcts of the Kidney.—The peculiar manner in which the interlobular arteries of the kidney terminate almost without anastomoses in the efferent vessels of the glomerules is particularly predisposing to the retention of whatever emboli enter them. For this reason single and multiple, mechanical and infectious, emboli are all very frequent in the kidneys.

Anemic Infarctions.—These result from embolism of arteries which have no anastomosis by which collateral circulation can be established and the integrity of the tissue maintained.

The anemic infarct is one of the easiest conditions to recognize. To the naked eye, according to its age, it appears as a slightly elevated, distinctly circumscribed, pale-colored area, distinctly visible beneath the capsule; or when older, as a depressed, contracted, circumscribed, pale-yellow, gray, sometimes nearly white area. When incised, this superficial area is found to be the base of a conic-shaped area of degenerated tissue, the blood-supply of which has been shut off by an embolus lodged at the apex of the cone or a little beyond it. The infarct is usually surrounded by a red line that corresponds to an inflammatory reaction in the healthy tissue surrounding the infarct. If the tissue be examined microscopically, it is found that the anemic tissue first shows a cellular change resembling cloudy swelling, but that it soon falls into a condition of coagulation necrosis in which the cells are represented by molecular débris containing the fibers of preëxisting connective tissue. In the course of time the reaction of the devitalized tissue upon the healthy brings about a proliferation of connective tissue which contracts and squeezes upon the infarct; this in turn becomes smaller and smaller from the absorption of its necrotic tissue until ultimately nothing remains. In time the surface of the kidney is pitted by a rather deep, somewhat stellate cicatrix, which, upon section, is seen to be produced by a thick band of cicatricial tissue extending more or less deeply through the organ, perpendicularly to the external surface.

Hemorrhagic infarction of the kidney differs from anemic infarction in that the infarcted tissue is saturated with blood which causes it to be dark red and swollen in appearance. The shape of the affected area is the same, and in the course of time the destruction of the erythrocytes, the transformation of their hemoglobin into hemosiderin, and the absorption of this pigment transform the originally hemorrhagic infarct into what is to all appearances an anemic infarct. The subsequent stages are the same.

Infectious embolism of the kidney adds to the described changes the lesions peculiar to the bacteria contained in the emboli—that is, abscess, tubercle, etc. The most frequent infectious emboli come from the cardiac valves in malignant endocarditis, and in most cases carry with them pyogenic bacteria. Metastatic abscesses result, and the infarction is ultimately entirely obscured by suppuration.

Miliary metastatic abscesses result from the dissemination through the blood of minute infectious emboli—single bacteria or small groups of them. These, when retained in the kidney, produce small focal inflammations—*miliary abscesses*. They vary in size from the smallest dot to a millet seed, and usually occur about the small veins or in the capsules of the glomerules. Sometimes the bacteria grow in masses in the capillary loops of the glomerules and obstruct them, at times causing an accumulation of cellular exudate in the surrounding spaces and destruction of the epithelial covering of the glomerules. Ultimately a minute focus of purulent infiltration is found to surround the entire glomerule, extending from it in all directions, and invading the interlobular tissue. The epithelial cells in the tubules contiguous to the inflammatory area show marked changes, and many undergo necrosis and are desquamated. The pus-cells may invade the tubules themselves, and some may escape with the urine.

The majority of these little abscesses no doubt heal by the simple absorption of the cells and destruction of the bacteria. Sometimes they spread and lead to suppuration and destruction of the entire organ, producing a lesion similar to the so-called *surgical kidney*. The escape of the bacteria through the kidney into its pelvis, or the extension of the inflammatory process directly to the pelvis of the kidney, leads to the condition known as *pyelonephritis*.

Pathologic Physiology.—The function of the kidney is impaired according to the extent of the lesions present. As, however, considerable portions of the secreting substance of both kidneys can be removed by experiment or disease without material danger from impeded excretion, no important constitutional symptoms may be observed.

The urine may contain some blood and albumin which enter from the diseased areas. In cases of abscess formation, pus may be present in the urine.

Nephritis; Inflammation or Degeneration of the Kidney; Bright's Disease.—The kidneys form the chief avenues for the elimination of many toxic substances dissolved, but not destroyed, in the blood. Through their delicate capillary glomerules and tubular epithelial cells pass the greater part of the surplus water and effete materials of the body. No better illustration of the importance and activity of the organs is necessary than that furnished by the observation of the suspension of their function in the course of *Bright's disease* or *nephritis*.

The true nature of nephritis is not known. The cases vary, some appearing purely degenerative, others more distinctly inflammatory in nature, depending upon the variety, severity, and duration of the case. One must bear in mind, however, that the kidney is an organ almost purely parenchymatous in structure, so that its inflammatory lesions differ from those of organs rich in connective tissue; also that the function of the organ, being essentially excretory, the tendency is for its cells to take up from the blood those very substances that produce the degenerative changes.

Etiology.—A more or less marked nephritic change occurs in nearly all the infectious diseases, where it may depend either upon the presence of micro-organisms in the substance of the organ, as in septicemia; upon the elimination of toxins from the blood, as in diphtheria; or upon the general systemic disturbances due to high fever and altered metabolism. Toxic substances, such as cantharides, turpentine, phosphorus, etc., produce marked alterations of the kidneys, beginning in hyperemia and ending in degeneration.

One of the first indications of damage is found in the presence of serum-albumin in the urine, as well as in the fact that the function of the organ is disturbed, so that a diminution in the urinary excretion occurs.

Acute parenchymatous nephritis, acute nephritis, acute hematogenous degeneration of the kidney, or **acute tubular nephritis,** is one of the renal diseases in which certainty of classification fails. It is a parenchymatous disease with all the appearances of cellular degeneration, but at the same time is accompanied by congestion and various cellular changes that make it appear as an inflammation. Its degenerative character is, furthermore, shown by the fact that it accompanies or follows conditions predisposing rather to degeneration than to inflammation.

Etiology.—The disease sometimes occurs in individuals whose apparently normal condition affords no explanation for it. More frequently, however, it occurs in those already suffering from such constitutional disorders as diabetes, gout, icterus, etc.; or in those acutely ill from the infectious diseases, especially diphtheria, scarlatina, variola, measles, croupous pneumonia, typhoid fever, erysipelas, septicemia, pyemia, sapremia, cholera, acute inflammatory rheumatism, yellow fever, relapsing fever, etc.

It also occurs after the ingestion of certain poisons, such as corrosive sublimate, arsenic, phosphorus, cantharides, petroleum, chromic acid, etc.

These facts explain the tendency to consider the lesion a toxic degeneration rather than an inflammatory condition, for in all the causes mentioned it probably results from the endeavor to eliminate some poison circulating in the blood.

Cold and exposure, which at times seem to be exciting causes of the affection, may operate solely by increasing the functional activity of the organs to so marked a degree that an intoxication through which the patient might have passed in safety, becoming doubled in its intensity, acts destructively upon them.

The *morbid anatomy* of acute parenchymatous nephritis will vary according to the degree of damage done. Indeed, the changes found in fatal cases may appear so insignificant that one is tempted to think the organ normal. More frequently, however, the kidneys are more or less enlarged, sometimes even to double their normal size. They are usually congested, red in color, feel softer than normal, and are more or less edematous. The capsule is smooth and loose.

When incised, the organs are usually juicy, bloody fluid escaping and obscuring the cut surface, upon which bleeding vessels can be seen. When the cut surface is freed of blood by scraping or washing, a marked difference between the cortical and medullary portions is observed.

The cortex is usually pale gray or grayish-red in color, while the medulla is dark red. The pale color of the cortex depends upon swelling of the affected cells and the pressure they exert upon the capillaries that are emptied, so rendering the cortex anemic. The less marked swelling of the cells and the larger size of its vessels permit the medulla to remain congested. A yellowish tinge of the cortex usually depends upon fatty change of its cells.

When the cut surface is closely examined, the glomerules may be distinctly seen as red dots. If, however, they are not congested or their capsules filled with inflammatory exudate, it may be impossible to see them. The capsule of the organ strips off readily, leaving a smooth, pale, purplish, shining, translucent surface, marked with small veins.

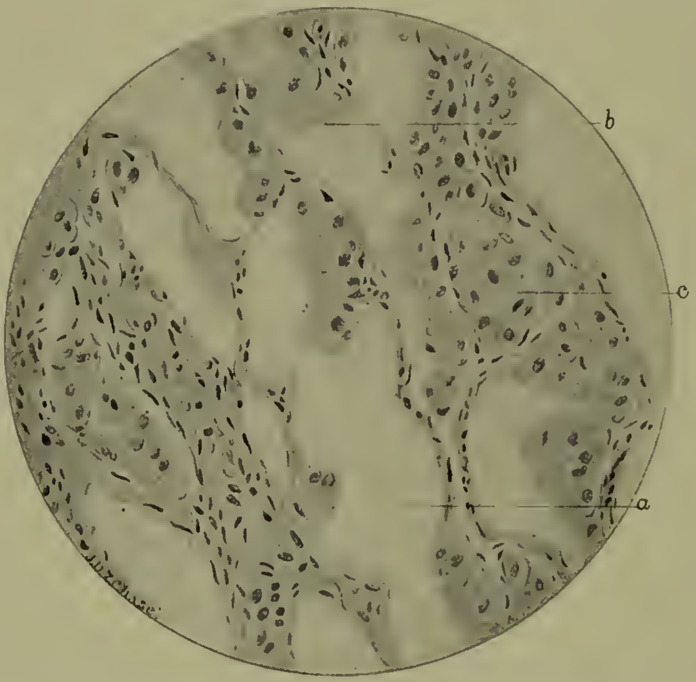

FIG. 337.—Acute parenchymatous nephritis (catarrhal): *a*, Tubule denuded of a large part of its epithelium; *b*, cells in a condition of degeneration; *c*, mass of desquamated cells in a tubule.

In very pronounced cases the cortical substance may contain small, irregularly shaped, scattered, whitish or yellowish areas of irregularly distributed fatty metamorphosis of the cortex. When considerable fatty metamorphosis is present, little fat-droplets appear upon the moist cut surface of the kidney.

Pathologic Histology.—The *microscopic appearances* and distribution of acute nephritis also vary in different cases, sometimes seeming to affect chiefly the glomerules (*glomerulonephritis*), sometimes being chiefly seated in the convoluted tubules (*tubulonephritis*), and sometimes affecting all the parenchymatous substance.

When the *glomerules* of the kidney are most markedly affected, the lesion is called *glomerulonephritis*. It is most frequent in scarlatina and diphtheria. The capsular space is usually filled with inflammatory products, consisting of desquamated and more or less degenerated glomerular and capsular epithelium, leukocytes, erythrocytes, and granular matter, mostly albuminous, though sometimes fibrinous in nature. The cells may show a granular degeneration, or may be in a condition of fatty metamorphosis. If the destructive processes have not progressed too far, it may be found that proliferation of the epithelium has preceded desquamation and necrosis. This will be shown by the presence of karyokinetic changes which indicate regenerative efforts at the replacement of lost cells. The number of erythrocytes is variable, and may be taken as an indication of the extent of the vascular injury. The escaped blood fills up whatever space remains within the capsules, and flows down the tubule, where it coagulates in little cylinders corresponding to the interior of the tubule. Here are formed the "blood-casts" sometimes found in the urine.

The glomerular capillaries may be full of blood, or may contain many leukocytes. Very frequently larger cells with fatty degenerated protoplasm and fragmented nuclei are found within the capillaries. These somewhat resemble fatty degenerated leukocytes, but are probably detached and degenerated endothelial cells.

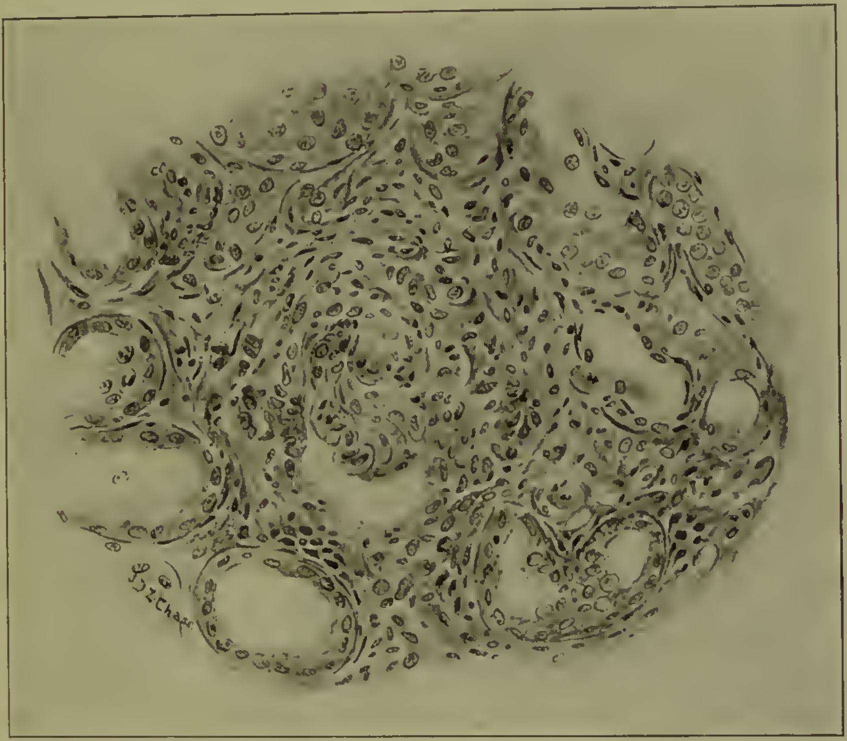

FIG. 338.—Acute parenchymatous nephritis, scarlatinal variety. The illustration shows a glomerule whose capsular space is nearly obliterated by an accumulation of leukocytes, desquamated epithelium, proliferated epithelium, and cellular and fibrinous exudate. Most of the tubules in the immediate neighborhood were nearly normal.

Disease of the glomerules alone is a rare condition. More frequently combined glomerular and tubular changes are present, and in the common form of parenchymatous nephritis the majority of the glomerules escape, while the tubules suffer. For this reason the term *acute tubular nephritis* has sometimes been used. By most clinicians and pathologists, however, the cases are known as *acute parenchymatous nephritis* or *acute catarrhal nephritis*, according to the variety of change present. The uriniferous tubules are more frequently affected high up—that is, in the convoluted tubules—than elsewhere, though in the particular form know as *catarrhal nephritis* the epithelium as far down as the collecting tubules is profoundly altered, and frequently desquamates, leaving the tubules bare.

The cellular changes observed in the tubules of the kidney vary according to the kind and severity of the process. Thus, in the intoxication of diphtheria, ricin, abrin, cantharides, chromic acid, and corrosive sublimate, there may be more or less localized necrotic foci, which become apparent upon microscopic examination as areas in which the cells no longer stain well and in which the nuclei are fragmented. The irregular-sized, scattered, nuclear fragments frequently show a marked affinity for certain stains, notably methylene-blue. The protoplasm of the necrotic cells may be granular or hyaline, sometimes splitting up into irregular hyaline blocks.

In a far greater number of cases the action of the circulating poisons causes a more general process, involving parts or even the whole length of the tubules.

In mild cases the cells, chiefly of the convoluted tubules, show cloudy swelling ; or the cloudy swelling may involve nearly every cell in the kidney, extending the whole length of the tubules. In more severe cases the cellular change is fatty, the metamorphosis being first observed in the convoluted tubules, next in Henle's tubules, and lastly in the collecting tubules.

When the cells of the kidney are in a state of cloudy swelling, the organ is translucent, grayish, anemic, and somewhat enlarged; when fatty, the yellowish color of the fat is distributed in streaks and spots throughout the kidney.

Microscopically, cloudy swelling causes the cells to appear enlarged and abnormally granular. They may show retrogressive changes of the nucleus. Sometimes a hydropic condition is added, so that the protoplasm becomes vacuolated. The cells usually remain attached to the basement-membrane. Fatty degeneration when present is unmistakable, though sometimes the occurrence of small pigment-granules in the cells may occasion some doubt. The fatty change is most noticeable in the convoluted tubules, but may also occur lower down.

Nephritis, in which the cells are desquamated and removed from the kidney, is described as *catarrhal* or *desquamative*. The cells escape with the urine, but may be so altered by the disease that when subsequently found in the urine they may be unrecognizable. To such fatty degenerated cells the name *compound granule cells* is frequently applied.

In such cases an effort at regeneration is manifested by karyokinetic changes in the nuclei of the remaining cells, so that after severe attacks of acute parenchymatous nephritis, with marked destruction and desquamation of cells, the kidney may be completely restored.

In parenchymatous nephritis the cells are the chief structural elements affected, but cases studied microscopically always show some changes of the interstitial tissue and are accompanied by the collection of products of inflammation in the tubules. These usually form cylinders that are described as urinary cylinders, or more familiarly as *tube-casts*.

Tube-casts are of various composition. They sometimes consist of perfectly transparent hyaline substance, supposed to be similar to fibrin, and are then called *hyaline casts*. Their substance is adhesive, and to them adheres molecular matter resulting from cellular degenerations, pigment molecules, minute crystals, desquamated renal cells, leukocytes, etc.

Blood-casts are formed by the coagulation of extravasated blood in the uriniferous tubules. Sometimes the entire epithelial lining of a tubule is desquamated for some distance, and succeeds in escaping from the tubule, forming *epithelial casts*. Sometimes hyaline casts are called epithelial when epithelial cells adhere to them.

The parenchymatous degeneration of the renal cells also seems to result in the exudation from their cytoplasm of minute granules, which collect in the tubules and form more or less complete moulds, which, when later observed in the urine, are known as *granular casts*. When these are composed of very fine molecular matter, they are usually specifically denominated *pale granular casts.* When the granules are coarse and are not so much the result of the conglomeration of albuminous as of fatty molecules, the larger darker granules form *dark granular casts.* In chronic nephritis, both parenchymatous and interstitial, but especially in the interstitial form and in amyloid disease, a peculiar, solid, translucent cylinder of slightly yellowish color and slightly brittle consistence is occasionally seen—the *waxy cast.* Sometimes these react typically to the iodin test for amyloid substance.

A microscopic study of the urine in nephritis is of extreme diagnostic importance, as by it only can be discovered what form of kidney disease exists; and very often a correct judgment of the nature and extent of the process can be ascertained from such an examination.

In acute parenchymatous nephritis there are few alterations outside of the glomerules and tubules of the kidney. In cases in which the changes are acute and the kidney considerably swollen, distended vessels, edema of the cellular tissue, and occasional fibrin and corpuscular deposits are observed in the stroma of the kidney. These serve to separate the tubules, and may lead one to infer that the connective tissue is hyperplastic. The inflammatory edema is probably infectious in origin.

When this condition is marked and the round-cell infiltration is considerable, the term *inflammatory edema* is used to describe it. The cellular infiltrations are usually observed near the capsule in the neighborhood of the vena stellata and along the lines of the interlobular veins. There are frequent infiltrations in the boundary layer of the cortex.

In diphtheria these cellular infiltrations are extremely common, and give the lesions a truly interstitial character. The cells are in part leukocytes, in part lymphocytes, but in large part plasma cells.

Acute parenchymatous nephritis may terminate in perfect recovery, or may recur and lead to conditions known clinically as *subacute nephritis;* or by frequent relapses may become chronic. Many of the severe cases terminate fatally.

Pathologic Physiology.—The interference of acute parenchymatous nephritis with the function of the kidney varies according to the extent of the changes present.

In wide-spread glomerulonephritis the accumulation of the inflammatory products in the capsular spaces and the destruction of the glomerules may entirely suppress the secretion of urine. The entire renal secretion being thus interrupted, the patient necessarily dies with the symptoms of uremia (*q. v.*). When the lesion is less wide-spread, the urine is diminished in quantity and altered in quality from the addition of the products of inflammation. It then becomes scanty, of high specific gravity, dark in color, and rich in salts and albumins. Microscopic examination shows the presence of blood corpuscles, pus corpuscles, desquamated epithelial cells, and, above all, the tube-casts already described.

When the disease is essentially situated in the tubules and their secreting cells are destroyed, the formation or elimination of urea is suspended and the condition becomes as critical to the patient as those cases in which no urine is secreted.

The retention of the urinary constituents within the blood occasions a variety of disturbances in other organs. Compensatory elimination is attempted by the alimentary apparatus, so that vomiting and diarrhea may occur. The cardiac pressure rises to aid the passage of blood through the kidney. The patient suffers from the auto-intoxication, and headache, visual disturbances, and convulsions occur. Convulsions are numerous in death from uremia.

In chronic nephritis, and especially in chronic interstitial nephritis, the occurrence of uremia and the death of the patient may be deferred for a long time, the system seeming to be able to accommodate itself to diminution of excretion.

Chronic Parenchymatous Nephritis.—It is a difficult question to decide whether cases of acute nephritis become chronic by repeated relapses of the acute form, or whether these supposedly acute cases with relapses have been essentially chronic from the beginning.

Chronic parenchymatous nephritis differs from the acute form in that it is clinically characterized by an insidious onset and by comparatively mild symptomatology. It is, however, subject to frequent acute exacerbations in which the destruction of the kidneys probably progresses rapidly.

Etiology.—The etiology of the disease is very obscure. It is supposed to depend upon the continuous excretion of irritating metabolic products, and is to be looked upon as a disease of elimination.

It is progressive and probably does not recover, but either terminates fatally during one of the exacerbations, or changes by increase of the connective tissue so as to resemble chronic interstitial nephritis. The essential lesions are chronic degeneration of the parenchyma and progressive increase of the connective tissue.

Morbid Anatomy.—The macroscopic changes are varied. The typical appearance is familiarly known as *large white kidney*, the organ being greatly increased in size and pale in color. Its consistence is softer than normal, though it may be loosely attached if the disease be not advanced.

The incised surface shows the cortex of the organ to be thickened and to vary in color, sometimes being uniformly yellowish, sometimes variegated by irregular mottling or striping of the normal parts with grayish-yellow or yellowish white. There may be small hemorrhages into the cortical substance. The medullary substance is usually congested and distinctly striped.

In other cases the enlargement of the organ is not very noticeable, and the pale color is absent.

Very chronic cases are characterized by the small size of the kidney, which has a granular surface, from contraction of intertubular connective tissue and loss of substance by degeneration. This, which probably represents contraction of an originally enlarged kidney, is called *pale granular kidney*, in contradistinction to the red granular kidney of chronic interstitial nephritis.

Pathologic Histology.—The microscopic features of chronic parenchymatous nephritis consist essentially of a fatty degeneration of the cytoplasm of the renal cells. There are great variations in the extent of this change, very considerable change being observed in cases in which the macroscopic lesions are pronounced; very little change in those cases in which the naked-eye alterations are few.

The fatty metamorphosis occurs in the epithelium of the glomerules and of the uriniferous tubules; also in the endothelium of the blood vessels. In addition to the simple degenerative changes observed in the parenchyma, there are found an appreciable amount of inflammatory edema and a slight degree of round-cell infiltration in the interstitial connective tissue. The greater the duration of the case, the more appreciable the changes in the connective-tissue stroma. In very chronic cases round-cell infiltration, hyperplasia with induration, contraction, and atrophy are found. These changes gradually cause the large white kidney to change into the white contracted kidney or pale granular kidney. In the atrophic stage the glomerules are destroyed one by one, and the related tubules atrophy.

The glomerules show a great variety of changes more or less closely resembling those of acute nephritis. The covering epithelium may proliferate or degenerate, the capsular space may be filled with the products of tissue growth or destruction, the endothelium of the capillaries may thicken, the cells alter their shapes, and the circulation be obstructed; or the endothelial cells and fibroblasts may form tissue masses which cause the glomerules to become fibroid. There is a distinct thickening of the capsular connective tissue about the glomerules, but never so marked as in the chronic interstitial nephritis. From the diseased glomerules inflammatory exudate may enter and collect in the capsular space and tubules in the form of hyaline, or more frequently granular, tube-casts.

The glomerules are frequently transformed into homogeneous or granular masses, this change seeming to be preceded by proliferative cellular changes that result in the closure of the capsular space, pressure upon the glomerule, and ultimate extinction of its nutrient supply.

The *tubular changes* consist of fatty degeneration and destruction of the secreting cells, which not infrequently detach from the basement-membrane and escape from the tubule before their dissolution is complete. This characterizes *chronic catarrhal nephritis*. The extent of the cellular destruction varies, being most constant and pronounced in the large white kidney. In kidneys with the variegated appearance the cellular changes are most pronounced in the fatty degenerated areas, while in glomerulonephritis practically no damage is done to the tubular epithelium.

The fatty change is seldom equal in all parts of the kidney, the chief ravages being in the convoluted tubules. Healthy or comparatively healthy tubules may be found close by those showing advanced fatty change. Fatty granules formed by the degeneration of the cells frequently collect in the tubules and form granular casts. These granules seldom consist exclusively of fat, cellular débris, leukocytes, erythrocytes, minute crystals, pigment-granules, etc., being also present. The cells of the tubules are pigmented, indicating disease elsewhere.

The *connective-tissue changes* consist of scattered areas of round-cell infiltration, more or less edema, and irregular fibroid proliferations in areas usually rich in cells. The fibrous change frequently affects the glomerular capsules and leads to thickening. There is little actual damage done the glandular substance by the contraction of the connective tissue, the reduction in size depending more upon atrophy than upon compression, the irregular granular surface depending upon atrophy of the tubular tissue.

The edematous and proliferated connective tissue may contain free fat-droplets or occasional leukocytes laden with fat-droplets resulting from cellular destruction.

Acute interstitial nephritis is usually of hematogenous origin, as in diphtheria, but may result from the extension of inflammation from the pelvis of the kidney (*pyelonephritis*) to the organ itself by continuity of tissue and conduction through the lymphatic vessels.

The micro-organisms known to be associated with it are the pyogenic cocci, the typhoid and colon bacilli, and the pneumococcus.

The micro-organisms enter the kidney as emboli, and lodge in the smaller vessels, especially the loops of the glomerules. In a short time the perivascular connective tissue becomes infiltrated with round-cells. If the embolus lodge in a glomerule, the round-cells may be present between its capillary loops, and also in the pericapsular areolar tissue. When the embolism takes place in some extra-glomerular vessel, the intertubular connective tissue becomes infiltrated, sometimes for a considerable distance along the course of the vessel. The irritation of the bacterial products soon acts destructively upon the neighboring renal cells, which undergo necrosis or fatty metamorphosis, and sometimes desquamate. The round-cells not infrequently crowd between the epithelial cells, enter the tubules, and appear in the urine.

The resulting damage may be slight, the kidney overcoming the bacteria and repairing the injuries by karyokinetic changes of the epithelium of the tubule or by scar formation after the pus has been absorbed.

When the process is active and much round-cell infiltration has occurred, actual dissolution of the tissue of the inflamed area and abscess formation may take place. In such cases evacuation into the tubules and subsequent cicatrization occur. The pus may also be absorbed.

In rare cases the pyogenic process continues and the entire kidney may be transformed into a sac containing pus (*surgical kidney*). This is, however, more frequent in cases originating from pyelitis (see Pyonephrosis).

Chronic Interstitial Nephritis.—This is a chronic affection of insidious onset, characterized by a progressive increase of the connective tissue of the kidney, accompanied by a gradual atrophy of the essential secretory elements.

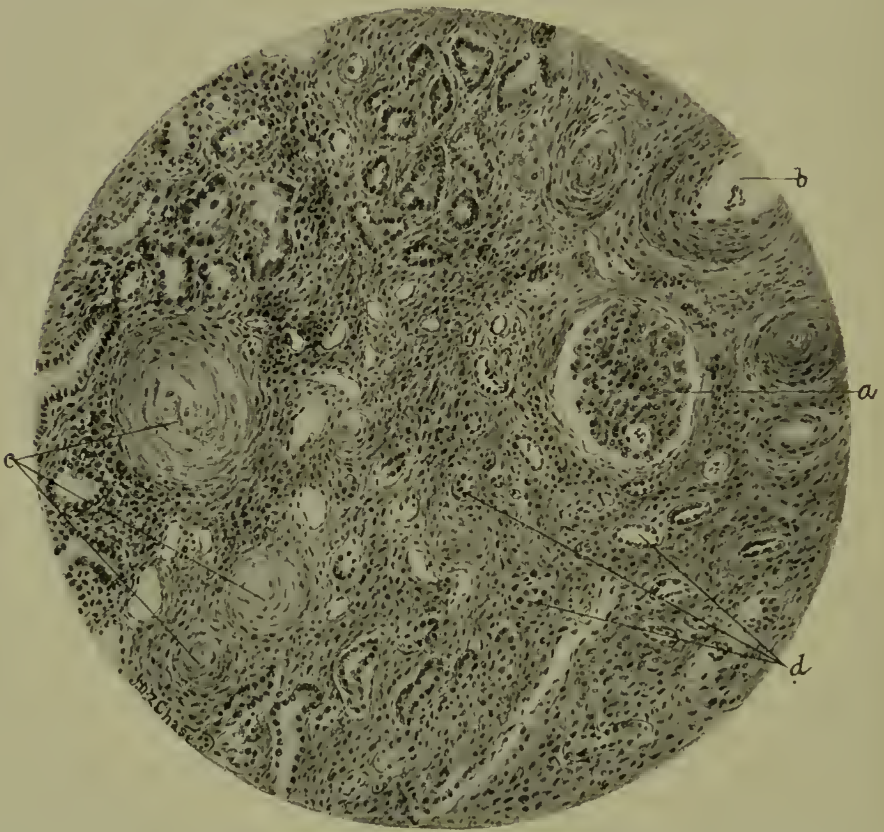

FIG. 339.—Chronic interstitial nephritis. The increase of connective tissue is almost universal: *a*, Functional glomerule with thickened capsule; *b*, greatly thickened capsule without glomerule; *c*, glomerule in different stages of contraction and extinction; *d*, tubules, some of which are atrophic.

The disease is characterized clinically by an increased quantity of urine of low specific gravity, with little or no albumin and very few tube-casts, of which the hyaline, pale granular, and waxy varieties only are found.

Etiology.—The cause of the disease is obscure. Some cases seem to follow attacks of the infectious diseases, some seem to follow definite intoxications, such as alcoholism, saturnism, etc., while others depend upon the irritative poison of gout and upon altered metabolic products the nature of which has not yet been determined.

Morbid Anatomy.—The kidney of chronic interstitial nephritis is small, dark red in color, firm in texture, and coarsely granular upon the surface—

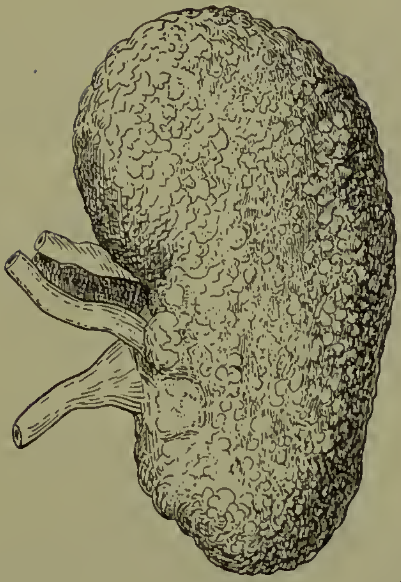

FIG. 340.—Granular and atrophic kidney (Orth).

red granular kidney or *granular contracted kidney*. The organ may be reduced to one-half its normal bulk. Its color may be modified by co-existing anemia, hyperemia, and fatty degeneration.

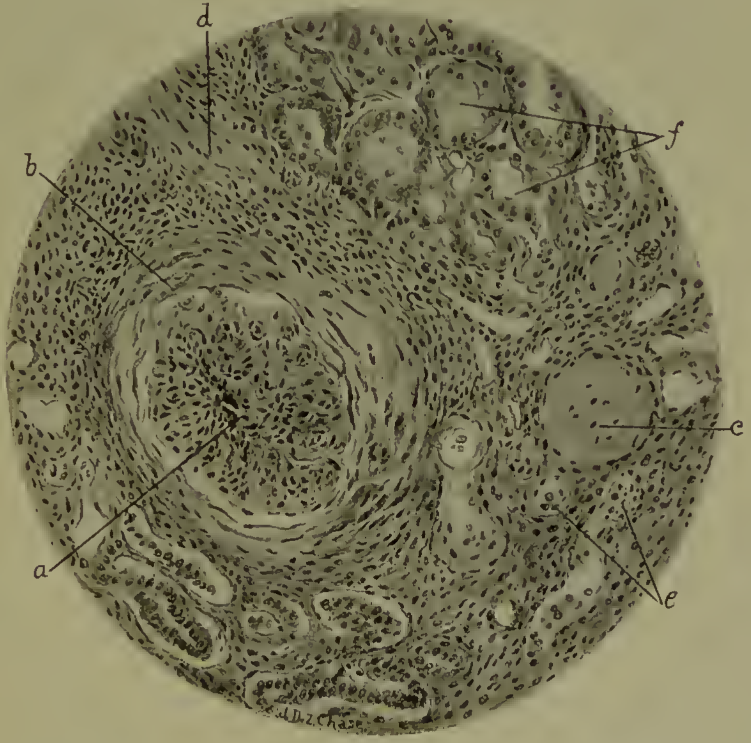

FIG. 341.—Chronic interstitial nephritis: *a*, Still functional glomerule with (*b*) mass of newly formed connective tissue surrounding Bowman's capsule; *c*, totally destroyed glomerule; *d*, newly formed cellular connective tissue; *e*, atrophic uriniferous tubules; *f*, slightly altered uriniferous tubules.

The firmness of texture depends upon the amount of connective tissue, the granular surface in part upon traction upon the capsule by internal cicatricial bands, and in part upon atrophy of the epithelial substance of the organ.

Cysts varying in size from a pin-head or smaller to a cherry, sometimes single, but more frequently multiple, may be observed upon the surface of the organ. These contain a straw-colored, sometimes watery, fluid. Rarely the contents are inspissated.

When incised, the appearance is striking. Marked disproportion between the cortical and medullary substance may be observed, the cortex appearing as a narrow rind or as a layer of irregular thickness, some areas being nearly normal in thickness, others very thin. Over the thinned areas the capsule is usually thickened. It is with difficulty that the division of the cortical substance into lobules by medullary rays can be made out. The cortical substance is likely to appear unusually homogeneous.

When an attempt is made to strip off the capsule, it is found intimately adherent—sometimes so adherent that scarcely any of it can be torn off without adhering kidney substance. In other cases the capsule strips quite readily from the more normal areas, but with great difficulty from those that are distinctly fibrous. The medullary substance of the organ usually shows little sign of alteration. In cases with marked retraction, in which the kidneys are reduced to one-half of their normal bulk, the medullary substance is also atrophic.

The Microscopic Appearance.—A great increase in the connective tissue of the organ is characteristic. There may be considerable lymphocytic infiltration. Some parts of the tissue show only a slight increase of the connective tissue, while others show marked increase, the connective tissue being dense and fibrillar and compressing and destroying the parenchyma.

The connective tissue is found in considerable quantity about the venules and glomerules ; to a less marked degree between the tubules. Every stage in the development of this tissue can be observed, but, as a rule, when the disease is sufficiently advanced to cause death, the tissue is for the most part of cicatricial density.

The destruction of the glomerules forms an important part of the histology of the disease. It occurs in part from the irritative action of substances brought to the glomerules by the blood, and in part from the compression of the glomerules by the thickened contracting capsules. In some cases the conditions point to a hematogenic influence only. In these the glomerule is somewhat infiltrated with round-cells, the covering epithelium being in a state of proliferation, of degeneration, and sometimes of desquamation. The capillary tufts are less well defined than normal, and the endothelium is swollen and altered in shape. From the glomerule an albuminous transudation occurs, with more or less distinct coagulation in the intracapsular space. Occasionally this deposition of coagulated fibrin occurs in a laminated form and entangles escaped leukocytes and erythrocytes from the capillary tuft. At other times the glomerule appears to be quite unchanged, while the contracting thickened capsule of Bowman obliterates all visible intracapsular space and presses upon the capillary tuft. Whatever the destructive process, whether partly due to intoxication, to arteriosclerosis, or to compression, the outcome of the process is the same, the glomerule being transformed to a structureless, granular, or homogeneous mass, at first somewhat lobulated, but from which eventually all trace of primitive structure disappears. The final absorption of the molecular matter and the contraction of the enormously thickened capsule lead to the formation of a fibrous nodule in the place of the original glomerule.

The tubules also suffer in chronic interstitial nephritis. In cases in which metabolic or toxic products cause the described alterations, the tubules frequently show signs of fatty change, such as are observed in chronic parenchymatous nephritis, though more limited in extent. The glomerules being destroyed, the tubules atrophy and appear collapsed, denuded, and contracted, so as to resemble capillary blood vessels.

Not infrequently groups of entirely normal tubules are found. Here and there dilated tubules and cysts of small size resulting from obstruction of lower parts of the tubules are present. Calcareous infiltration of the denser portions of the connective tissue and sometimes of the destroyed glomerules may be observed.

The disease occurs irregularly, all stages being present in nearly every kidney. It is probably on this account that the disease is of such long duration, the glomerules being destroyed one by one, their neighbors carrying on a vicarious function until the amount of remaining secretory tissue is insufficient to enable life to continue, and the patient dies of *chronic uremia* (*q. v.*).

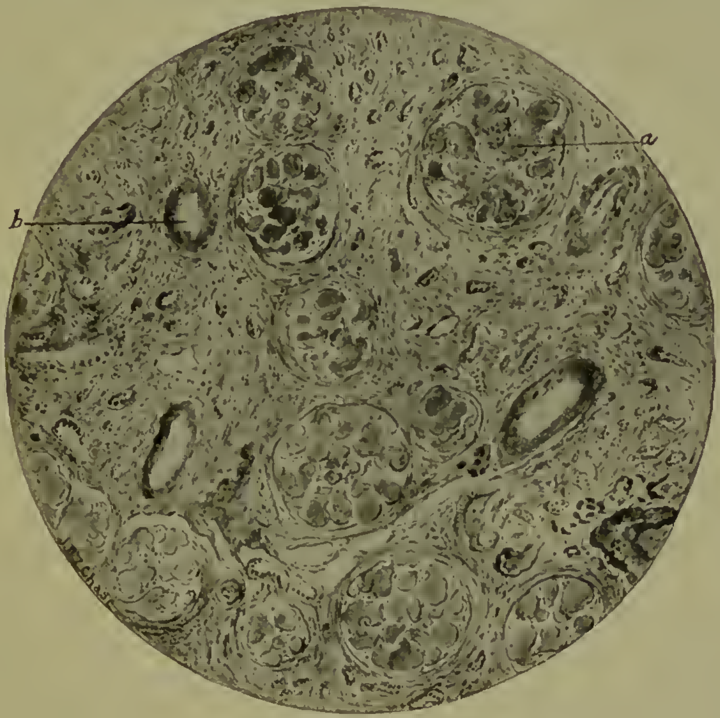

FIG. 342.—Amyloid degeneration of the kidney: *a*, Glomerule, showing degeneration of its loops; *b*, vessel with degenerated walls.

The healthy glomerules in such kidneys may appear considerably larger than normal and probably carry on a compensatory function.

Amyloid disease of the kidney is not infrequent and usually occurs with amyloid disease of other organs, though the kidney may first show the change. The disease manifests itself first in the small blood vessels, and is usually first seen in the glomerular tuft.

Morbid Anatomy.—The kidneys are frequently larger than normal. When but a slight degree of amyloid change is present, it may pass undiscovered. When marked and wide-spread, the organ may have the usual translucent appearance and may have lost much of its elasticity. The application of Lugol's solution of iodin to a section of amyloid kidney causes the dot-like, red-brown glomerules attacked by the affection to stand out conspicuously. When there is much associated parenchymatous degeneration of the organ, it may resemble the large white kidney.

The changes begin in single capillary loops and spread gradually until they embrace a number of contiguous loops, which subsequently unite and transform the glomerule into a homogeneous or nearly homogeneous mass, sometimes divided into more or less distinct lobules, with here and there a retained nucleus.

The disease spreads from the glomerule and vasa afferentia to other arterial and venous vessels, to the membrana propria of the tubules, and to the intertubular connective tissue. The amyloid substance is readily recognized by the usual color reactions with iodin and gentian-violet.

Amyloid disease rarely occurs in the kidney without damage of its parenchyma, as is shown by degenerative changes in the epithelial cells, not only of the glomerular covering and capsular lining, but also of the tubules. The cells sometimes detach and disappear, leaving denuded tubules with thickened amyloid walls, suggesting that the lining cells have themselves undergone the amyloid change. The tubules may contain casts of waxy, sometimes true, amyloid substance.

In nearly all cases of advanced amyloid disease of the kidney there is more or less chronic interstitial change, with a distinctly noticeable thickening of the capsule of Bowman and an increase of the intertubular tissue.

There may also be associated calcareous infiltration of the tissue.

SPECIFIC INFLAMMATIONS OF THE KIDNEY.

Tuberculosis of the kidney is rather frequent. It usually affects both kidneys, though in the chronic form it is, as a rule, more marked upon the one side than upon the other.

Miliary tuberculosis of secondary hematogenous origin is very frequent in pulmonary and other chronic forms of tuberculosis. It is caused by dissemination of tubercle bacilli through the blood, or by the simultaneous entrance of a number of bacilli into the blood, which eventually reach the kidneys. The lesions consist of scattered miliary tubercles that can be recognized with the naked eye as whitish, grayish, or yellowish dots upon the surface of the organ, frequently surrounded by a narrow zone of hyperemia. Their substance is solid and homogeneous, usually firm, and uniformly grayish or yellowish. The size varies according to the age of the lesions, which may attain the size of a pea. The number of tubercles varies: there may be a single one, usually they are few in number, but they may be very numerous. They are rather more frequent in the cortical than in the medullary substance, though they occur in both. Sometimes their distribution corresponds to that of certain blood vessels.

Microscopically, they have no essential peculiarities. The tubercles are typical in appearance. A zone of capillary congestion is often seen surrounding the lesion, and beyond this is an indefinite area of cloudy swelling and fatty metamorphosis of the parenchyma, congestion, necrosis, etc. The nodular shape of the tubercle is not always typical in the kidney, as the inflammation sometimes occurs along the intertubular spaces of the pyramids, and gives rise to caseous striation. Occasionally a tubercle forms in a glomerule.

Primary tuberculosis of the kidney is caused by tubercle bacilli carried by the organ through the blood vessels or through the lymphatic vessels from lower parts of the genito-urinary tract.

One or both kidneys may be affected. If the disease depends upon hematogenous distribution of tubercle bacilli, it is difficult to understand why both organs should so frequently be simultaneously diseased without tuberculosis elsewhere. The tubercle may form in any part of the kidney substance or in its pelvis. In the lymphogenous cases the primitive lesions are usually in the pelvis of the organ, in the pyramids, or in the calices.

Beginning as a miliary tubercle, the disease spreads steadily, invading new tissue by continuity and by lymphatic extension. Sometimes it limits itself to a lobe of the kidney corresponding to a pyramid and its cortex; sometimes it spreads and invades all parts of the organ. There is marked and extensive coagulation necrosis of the affected areas, which take on a yellowish or grayish-white color, and are homogeneous and of crumbly consistence. The necrosis terminates in softening and ultimate excavation of the extensively diseased areas, which evacuate into the pelvis, leaving ragged cavities. These may be as numerous as the pyramids themselves, and in many cases seem to correspond with them, so that a kidney of advanced chronic tuberculosis, when laid open by a longitudinal incision, shows in each half a series of irregular excavations or pockets in which the pyramidal substance seems to be scooped out.

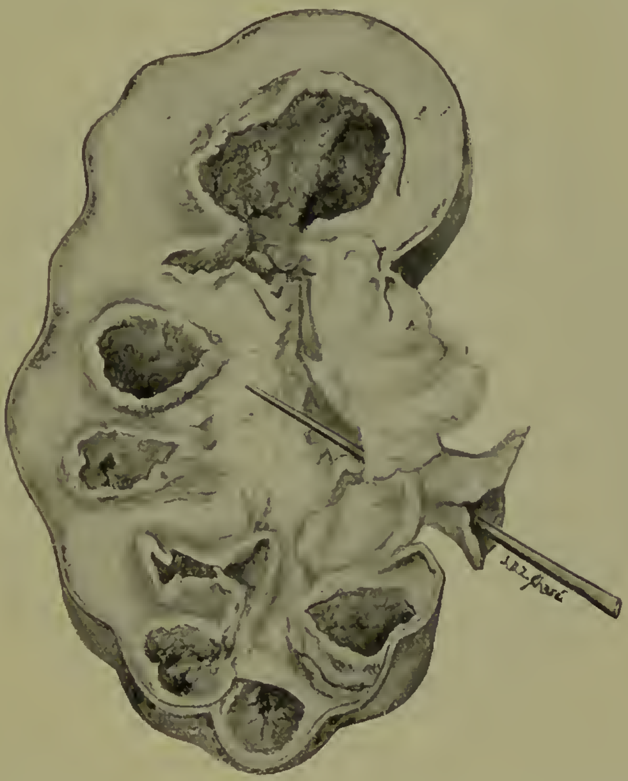

FIG. 343.—Tuberculosis of the kidney. The organ is viewed from the surface, exposed by a longitudinal section. The cortical substance is everywhere white and cheesy, the medullary portion, excavated. The pelvis is thickened, and a blow-pipe has been passed through the ureter so as to project into it.

It is scarcely possible for infectious material to be discharged into the pelvis of the organ without infecting it with tuberculosis, so that before the lesions of the kidney have grown large, the pelvis becomes thickened, opaque, ulcerated, and full of scattered tubercles. The pus and necrotic matter from the kidney and pelvis also usually infect the ureter, both directly through its mucous surface and by extension along the lymphatics, so that it soon shows more or less wide-spread tuberculous inflammation, becomes thickened, sometimes ulcerated, and not infrequently obstructed. The necrotic products from the kidney remaining and becoming diluted by the urine, some of which the organ may still be able to excrete, a considerable dilatation of the attenuated tissue of the diseased organ is occasioned—a *cold abscess of the kidney.*

In this way the kidney may be transformed into a large, thick-walled, grayish-white sac full of curdy pus. The remaining cortical tissue is usually necrotic and tuberculous. Microscopic study of the kidneys may reveal so little functional tissue as to make it remarkable that life could be so long sustained.

Syphilis.—Syphilitic lesions of the kidney are rare and vague. In hereditary syphilis fibroid induration of the organ, with marked contraction and deformity, is sometimes observed. The characteristic lesion, the gumma, rarely occurs. Healing, it leaves behind it the usual indurated, stellate, contracted cicatrix, but as similar scars frequently result from the organization of infarcts, caution is necessary in differentiating between them.

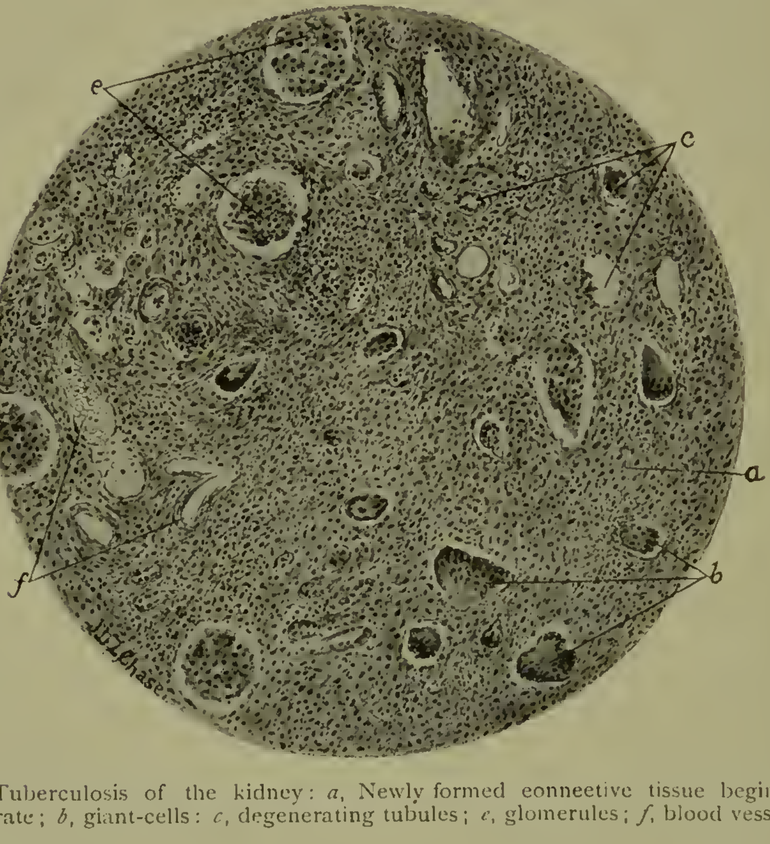

FIG. 344.—Tuberculosis of the kidney: *a*, Newly formed connective tissue beginning to degenerate; *b*, giant-cells: *c*, degenerating tubules; *e*, glomerules; *f*, blood vessels.

Lepra, glanders, and actinomycosis very rarely show manifestations in the kidney.

Tumors of the Kidney.—**Connective-tissue tumors** of the kidney are rare.

Fibroma occurs in the form of minute, rarely large nodules, varying from the size of a pinhead to that of a pea. It may occur in any part of the organ, pushing aside the renal tissues as it grows. The tumor is easily confounded with cicatrices, but is usually distinctly circumscribed, while the cicatrices radiate into the surrounding tissue.

Myxoma, lipoma, angioma, and various combinations of the simple tissue tumors are occasionally seen, but are usually small and unimportant. The tumors may be situated in the kidney substance, in the capsule, or in the pelvis.

Sarcoma is more frequent, and is one of the most important renal tumors. The greater number are either congenital or make their appearance in the first months of life. They form tumors of considerable size, consisting of soft, whitish, vascular, medullary tissue masses which may conform more or less to the kidney in shape, but are usually irregular and cause the organ to lose its morphologic characteristics. The tumors may consist of round- or spindle-cells or of both, and very frequently contain large spindle-shaped muscle-cells having transverse striations. When such cells are present, the tumor is called *rhabdomyosarcoma*, sometimes simply *rhabdomyoma*. These tumors, as Ziegler points out, probably originate early in embryonal life. The congenital sarcoma is likely to be very vascular, and, like other telangiectatic tumors of the kidney, may occasion considerable hematuria.

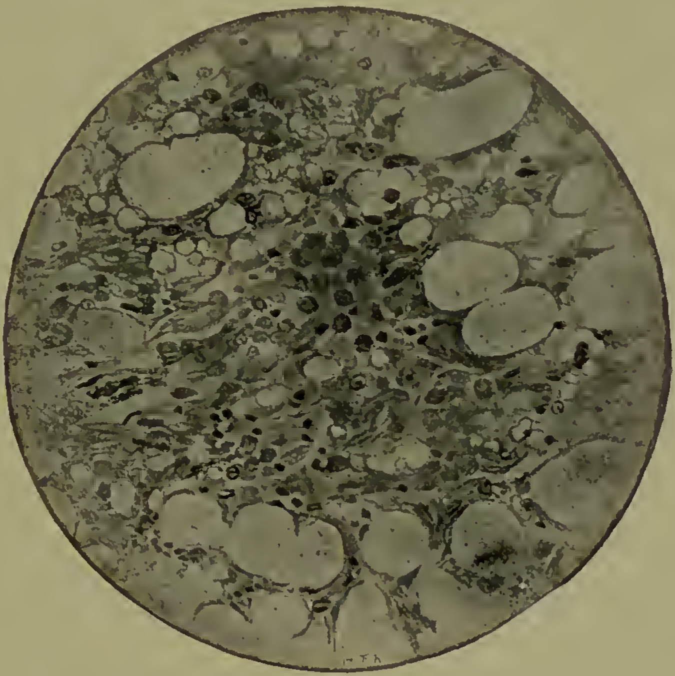

FIG. 345.—Hypernephroma of the kidney, showing the indefinite structure and the presence of considerable fat. This section passed through the center of the main tumor nodule (Zeiss, Oc. II., Ob. D. D.).

Sarcoma of the kidney may also occur later in life, when it appears as more or less rounded nodes, sometimes well circumscribed. They are usually quite vascular, many of them true *angiosarcomata*. The so-called *perithelioma*, which grows from the perithelial tissues of the vessels, is also of not infrequent occurrence in the kidney.

The tendency of renal sarcoma differs in the congenital and acquired varieties. The former is exceedingly malignant, growing rapidly, disorganizing tissue, and causing death, while the latter may be slow in development, limited to the kidney, and give no metastasis for a long time.

Epithelial Tumors.—Under the name of *strumæ lipomatodes aberratæ renis* Grawitz has described small pea- or cherry-sized subcapsular growths of the kidney, consisting essentially of tissue originally derived from the adrenal body and included in the kidney substance as it develops. These tumors are now known as *hypernephromata*.

The tumors usually form circumscribed whitish masses, and were formerly mistaken for lipoma and carcinoma. Microscopically, their structure is irregular, like that of the adrenal body. There is a connective-tissue framework with numerous cells arranged in nests and columns. The cells contain fat and glycogen, and closely resemble those of the adrenal body. When small, they may remain unnoticed, but some of them take on rapid growth, extensively infiltrate the surrounding tissues (more frequently the surrounding than the renal tissues), and may occasion metastatic secondary growths. These cases not infrequently cause death.

Adenoma is rare. It forms sharply circumscribed whitish nodes, varying in size from a pin-head to a walnut, and is composed of glandular alveoli, resembling the adenoma of the ovary. Many of the alveoli show a tendency toward the formation of papillary excrescences; some are distinctly papillary. The tumor is benign, but it is thought capable of changing its disposition when proper conditions exist. The tumor is supposed to develop from the uriniferous tubules of the kidney, the alveolar form probably originating from convoluted tubules, the cystic and papillary forms, from the collecting tubes. Many of the tumors formerly described as adenomata were probably hypernephromata.

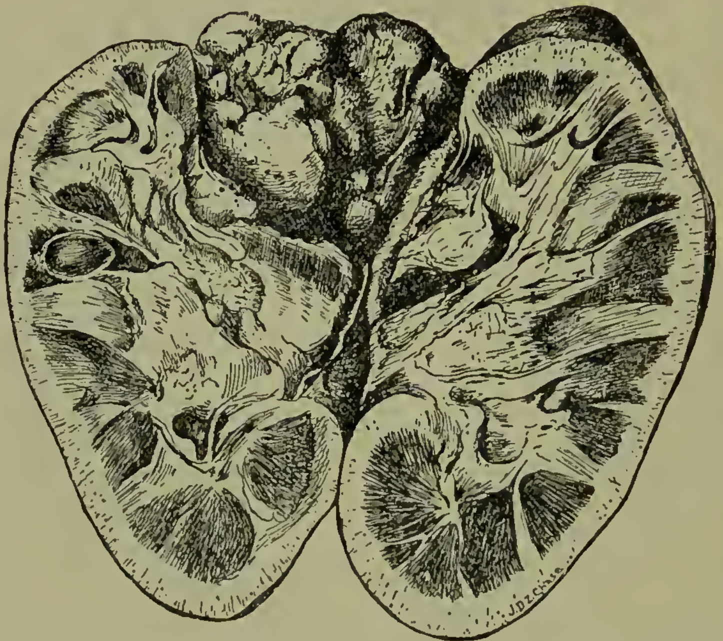

FIG. 346.—Hypernephroma of the kidney. Organ split longitudinally, and showing the tumor in the upper left-hand half.

Carcinoma of the kidney is rare. When small, the tumor may invade a part of the renal substance and be fairly well circumscribed, but when large, it invades it extensively and transforms it into a tumor mass which may continue to conform in outline to the kidney itself. The organ may be increased in size so as to equal the bulk of a cocoanut. The tumor usually does not infiltrate surrounding tissues, though it nearly always embraces the pelvis. When the organ is incised, the capsule is found thickened, the substance differentiated into nodes, in which the tumor is actively growing, and into more or less well-marked intermediate areas, rounded or irregular, in which mucous degeneration is in progress. No kidney substance can be found. Hemorrhages into the tissue are common. Unlike carcinoma elsewhere, renal tumors are more frequent in childhood that in later life, but they occur at all ages. It may be that some of the renal carcinomata of childhood are hypernephromata that have taken on malignant development. Renal tumors are nearly always unilateral, but cases of simultaneous bilateral carcinoma are on record.

The tumors are not prone to give early metastasis.

Cysts of the kidney are common. They may be single or multiple, and vary in size from a pinhead to a walnut. They may occur in exceptional cases and singly, in otherwise normal organs, but are much more frequent in kidneys affected with structural alterations, associated with or followed by obstruction of the tubules. Among these may be mentioned collections of urinary salts in the organ, tube-casts obstructing the tubules, cicatrices from infarcts, etc., compressing the tubules, inflammatory conditions of the pelvis extending to the pyramids and obstructing or obliterating the tubules, chronic interstitial nephritis, and arteriosclerosis.

The cysts are formed in consequence of the continued excretion of urine after tubular obstruction, and are, therefore, simple retention cysts. They usually result from distention of a single tubule, though when a number are closely approximated, they not infrequently seem to unite. The cysts are always lined with epithelium, which usually has a flattened, almost squamous appearance. The contents may be clear and watery, urinous, inspissated, or even colloid.

Cysts frequently form in intra-uterine life through various abnormal conditions, and are then very numerous and destructive, because of the atrophy of intermediate renal substance caused by the pressure of the fluid within them. The organs are sometimes so enlarged by the cystic distention as to cause an abdominal enlargement that may interfere with birth.

Cystic kidneys similar to the congenital form are often found late in life in patients that may or may not die of uremia. The organs are usually increased to one and one-half times or twice the natural size, and are made up almost entirely of cysts and intermediate fibrous septa in which scattered renal elements are found. Such cases are usually looked upon as congenital in origin, though one cannot be certain that they were not formed in after-life. The cysts cause no inconvenience so long as the amount of remaining kidney substance is adequate to maintain life. When, however, the atrophy of the intermediate substance exceeds a certain limit, uremia and death must follow.

Hydronephrosis.—A cystic dilatation of the entire kidney frequently results from obstruction of the ureter. This is called *hydronephrosis* or *hydrops renalis.* Various obstructive changes of the ureter are observed. Among them are calculi, strictures following inflammations, fold of mucous membrane, twists and kinks of the ureter, the pressure of enlarged organs, morbid growths, diseases of the bladder obstructing the outlet of the ureters, phimosis, enlarged prostate, stricture of the urethra, and other conditions making evacuation of the bladder difficult and thus remotely influencing the escape of urine from the ureters.

The retained urine distends the ureter when the obstruction is near the bladder, and then extends to the pelvis, which gradually yields, and by its lateral traction opens the hilum of the kidney, dilates the calices, and in the course of time by combined traction, distention, and atrophy, transforms the organ into a sac in which is contained a larger or smaller collection of liquid —sometimes as much as from 5 to 10 liters—and in the wall of which little or no remaining kidney substance can be found.

The fluid at first consists of urine, without much alteration from the normal. So long as kidney substance is present in the sac, the secretion of urine continues and there is no important change in the fluid. When, however, secretion ceases, the fluid changes its character and becomes watery. This is followed by deposition of the salts of the urine in the form of an incrusting layer within the cyst. I have seen a case in which the kidney in hydronephrosis became as large as a man's head, and consisted of a sac of attenuated fibroconnective tissue in which no renal structure was any longer visible. Its interior was incrusted with phosphate of calcium and magnesium until a layer had formed, the thickness of which was nowhere less than $\frac{1}{4}$ inch, and in many places exceeded $\frac{1}{2}$ inch. The contents of the cyst may be modified by such accidental conditions as hemorrhage and infection. When the kidney is transformed into a sac with purulent contents, the condition is described as *pyonephrosis*.

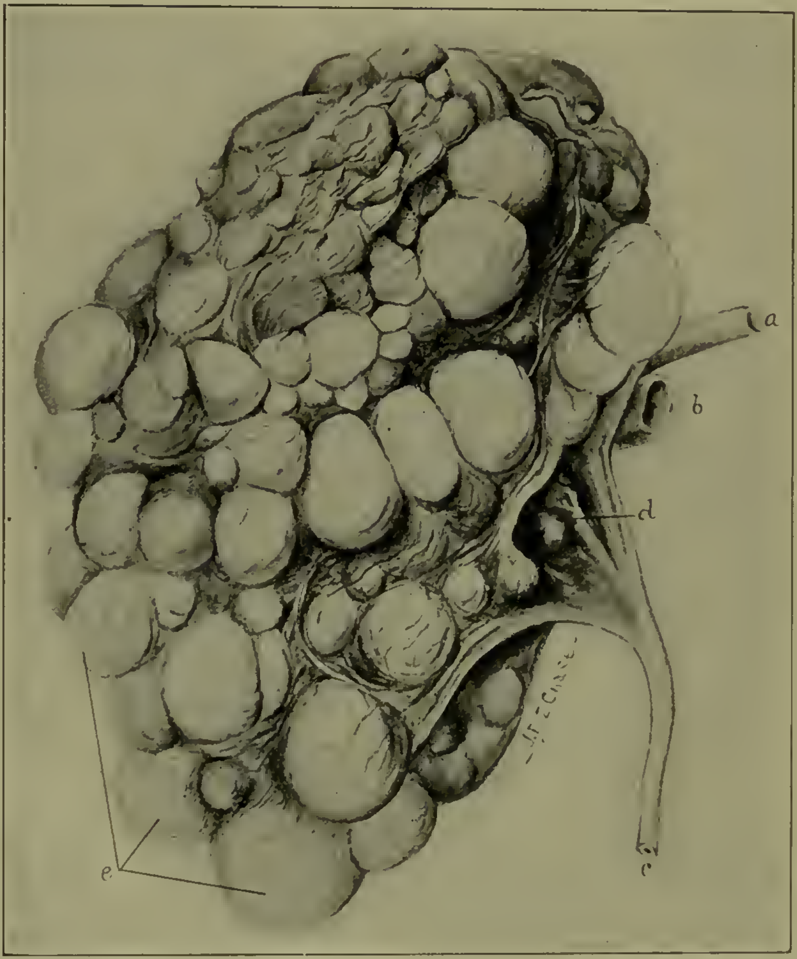

FIG. 347.—Congenital cysts of the kidney: *a*, Renal artery; *b*, renal vein; *c*, ureter; *d*, pelvis of the kidney; *e*, cysts filled with clear fluid.

Hydronephrosis is usually unilateral, but may be bilateral when the obstruction causing it can operate upon both ureters, as when they are compressed by a pregnant or diseased uterus, or when the escape of urine from the bladder is obstructed by an enlarged prostate, stricture of the urethra, or phimosis.

DISEASES OF THE PELVIS OF THE KIDNEY AND OF THE URETER.

Pyelitis, or inflammation of the pelvis of the kidney, occurs in typhoid, scarlatina, variola, pyemia, cholera, diphtheria, and other infectious diseases, in some intoxications, especially those in which the elimination of the poison occurs through the kidneys, as catharides, turpentine, and cubebs. The affection is catarrhal, rarely pseudomembranous, and the tendency is to recovery as soon as the cause is removed.

The most important forms of pyelitis result from local infection and from calculus.

Infection of the pelvis of the kidney is usually indirect. Some cases depend upon the retention of pyogenic bacteria excreted by the kidney during the course of infectious, especially pyemic, affections.

Many cases probably result from infection through the urinary apparatus. Pyogenic cocci are sometimes carried into the bladder with sounds and catheters, first producing inflammation of the bladder, and later ascending the ureters to produce inflammation of the pelvis of the kidney. Pyogenic cocci may also enter the bladder directly from the urethra in gonorrhea, or indirectly from pelvic abscesses, rectal inflammations, and inflammations of the uterus, vagina, and neighboring viscera, infecting the bladder contents and facilitating infection of the ureters and pelves of the kidneys.

Retention of urine with ammoniacal decomposition in the bladder favors bacterial growth, and in cases with distention it is easy to understand how micro-organisms can enter the dilated ureters and ascend to the pelves of the kidney.

The Bilharzia or Distoma hæmatobium, Eustrongylus gigas, Ascaris lumbricoides, filaria, etc., may produce pyelitis of varying grades of severity.

Morbid Anatomy.—Pyelitis may be catarrhal, hemorrhagic, pseudomembranous, suppurative, or ulcerative, according to the peculiarities of the case. Chronic forms, which are most destructive, usually depend upon calculus, tuberculosis, etc.

In the catarrhal form the mucous membrane is reddened, swollen, and dotted with punctiform hemorrhages. The exudation consists of desquamated epithelium and pus. The lymphadenoid tissue of the pelvis is increased. When diphtheritic in nature, a pseudomembrane forms upon the surface of the mucosa; when suppurative, pus forms in the pelvis and abscesses in its walls rupture either internally, leaving ulcers which heal by cicatrization, or externally into the perirenal areolar tissue, where abscesses of larger size—*perinephritic* or *paranephritic* abscesses—may form. Suppurative pyelitis easily extends from the pelvis of the kidney to the organ itself, leading to intertubular round-cell infiltrations, lymphogenic miliary abscesses, degenerations, dissolution of kidney substance, abscesses, and sinuses which form the excavations already described as *surgical kidney*. Should the ureter become obstructed, the collection of pus and urine in the pelvis causes dilatation and *pyonephrosis*. Abscesses may empty into the intestine, bladder, etc., by ulcerating through the walls.

Calculus.—When the pyelitis is occasioned by a calculus too large to escape through the ureter, the condition is somewhat modified, its cause being persistent and productive of traumatic injury. The lesions thus become chronic, ulcerative, and sometimes purulent. The extent of injury depends upon the size of the calculus and the infection accompanying it. The most extreme degree of local injury is seen in rare cases in which, because of atrophy of the entire renal parenchyma, the organ is represented solely by a thick connective-tissue mass surrounding a large calculus.

Calculi frequently cause hemorrhage by lacerating the delicate tissues.

Small calculi escaping from the pelvis of the kidney into the ureter have more or less difficulty in passing, so that their sharp projections may cause traumatic injuries of the mucous membrane, with more or less marked hemorrhage—the severe pain characteristic of *renal colic.*

Such stones sometimes become imbedded in the ureteral canal, through which they are unable to escape to the bladder, and become permanent obstructions to the outflow of urine. Calculi are usually unilateral, but may be bilateral.

In chronic inflammation of the pelvis of the kidney and of the ureter numerous small cysts sometimes occur upon the mucous membrane, probably resulting from the retention of secretion within small glands preëxistent or newly formed in the tissue (*ureteritis cystica*). Rarely, and especially in tuberculosis, there is a peculiar multiplication of the epithelium, with the formation of small bodies of a scale-like appearance analogous to cholesteatoma.

DISEASES OF THE BLADDER.

Congenital malformations of the bladder are not uncommon. Those most frequent are associated with inadequate development of the abdominal wall, by which prolapse of the bladder—*extrophy* or *inversion*—occurs. This condition may be associated with other forms of incomplete union, as epispadias (*q. v.*).

Abnormal communications between the bladder and pelvis, rectum and vagina, are not infrequent. In some cases the bladder has no outlet in the normal direction.

Rudiments of the urachus not infrequently remain in communication with or attached to the bladder, and may become dilated into a cyst with smooth walls and clear fluid contents. If the obstacle to urination develops early, the urachus may be dilated and patulous and serve as an outlet for the urine.

A few cases of double bladder are upon record. They may be situated side by side or one above the other. The ureters may empty into either or both of the sacs. Congenital diverticula somewhat resembling double bladders are rare.

The bladder may be entirely absent, the ureters then opening directly into the urethra. The bladder is sometimes so small that the urine must immediately pass from it into the urethra.

Hypertrophy of the bladder is rather frequent in consequence of obstruction to urination, and is seen in phimosis, stricture of the urethra, enlarged prostate, and vesical calculus. The wall of the organ becomes thickened from increase of its muscular substance, the columns of which are unusually apparent upon the inner wall. The mucosa is also thickened and often rugose, and together with the hypertrophy, signs of chronic inflammation resulting from ammoniacal decomposition of the urine, etc., are often present.

Dilatation of the bladder may be congenital or prenatal, and may depend upon atresia of the urethra. The bladder may be so enormously distended as to interfere with birth.

As an acquired condition it may depend upon obstruction of the outlet of the bladder or paralysis of the muscular walls of the organ. The obstructive dilatation that occurs in the adult is not an acute process, but one gradual in development and associated with hypertrophy of the muscular walls, which may reach 5 or 6 mm. in thickness. A dilated and hypertrophied bladder projects forward and may reach to the umbilicus. The paralytic dilatation is usually of rapid development, and is accompanied by marked attenuation of its walls. It is not infrequently followed by rupture, peritonitis, and death.

Rupture of the bladder may depend upon traumatic injury or occur from pathologic dilatation. The rupture is most frequent at the fundus posteriorly, and usually consists of a transverse laceration. Fatal peritonitis commonly follows. The traumatic injuries are most frequent in the neighborhood of the neck of the organ, and are succeeded by escape of urine either into the surrounding cellular tissue or externally. The escape of urine into the cellular tissue is particularly dangerous, as extensive phlegmonous suppurations are likely to follow.

Diverticula of the bladder are occasionally seen as acquired conditions. Their origin seems to depend upon accidental defects of the muscular wall of the bladder through which a small pouch of mucous membrane is enabled to enter during contraction. Sometimes no diverticulum is apparent so long as the bladder is relaxed, but so soon as pressure is brought to bear upon the organ, a sac consisting of the mucous membrane is forced through an opening in the muscular substance and projects upon the outside like a cyst, varying in size from a pea to an egg, depending upon the pressure exerted upon the bladder. The diverticula usually form inelastic, thick-walled pouches composed of hyperplastic peritoneum and mucosa, filled with stagnant, decomposing, and often purulent urine. They communicate with the bladder by rather small openings that may be ulcerated.

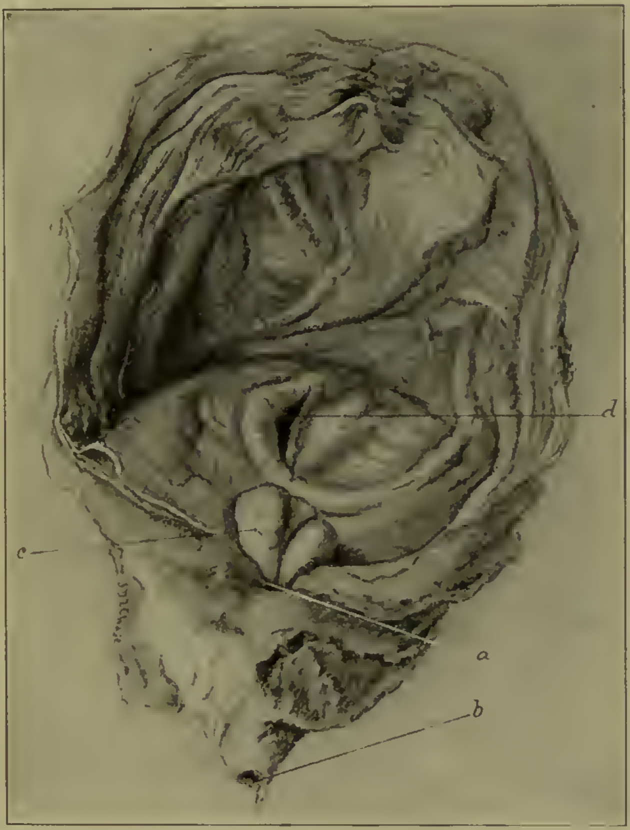

FIG. 348.—Hypertrophy of the bladder-wall: *a*, *b*, Inner and outer orifices of the urethra; *c*, enlarged prostate; *d*, opening the bladder into a diverticulum projecting posteriorly.

The stagnation of the urine within the diverticulum is a common cause of calculus formation.

The diverticula may be single or multiple, a few cases being on record in which they were very numerous, reaching as high as from 20 to 50 in number and varying greatly in size. They usually occur upon the posterior or lateral walls of the bladder.

Fistulous communications between the bladder and other viscera are frequent in the female and rare in the male. They usually result from necroses following prolonged pressure of the child's head upon the soft parts during delayed parturition, or from instrumental lacerations of the soft parts during delivery. Communications of this kind are known as *urogenital fistula* (*q. v.*). Traumatic fistulas between the bladder and vagina also occur after operative procedures for removal of the uterus and from pressure exerted by vesical calculi.

Fistulous communications between the bladder and neighboring viscera may occur in consequence of the ulcerations and necroses caused by malignant disease, suppuration, and traumatic injuries. In suppurative appendicitis the vermiform appendix sometimes establishes a communication with the bladder, through which it discharges its purulent contents.

Rectovesical fistulas permit the escape of the urine from the bladder into the rectum, or the entrance of fecal matter into the bladder. Gaseous evacuations from the rectum may also occur through the urethra *via* the bladder.

All communications between the rectum and the urinary organs are extremely dangerous, because of the liability of the urine becoming infected with organisms that may eventually reach the kidneys.

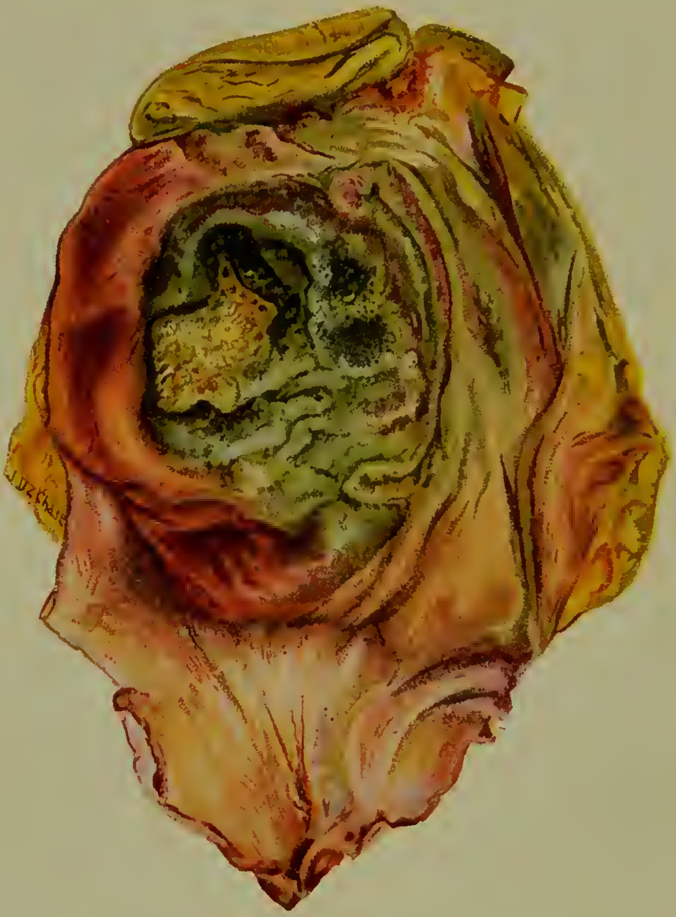

FIG. 349.—Gangrenous cystitis (Riesman).

Circulatory Disturbances of the Bladder.—**Anemia** of the mucous membrane and walls of the bladder is usually seen postmortem. The mucous membrane is white, and shows no injected vessels. As seen through the endoscope or speculum, however, the mucous membrane is rosy in color, so that it is probable that the pallor depends upon hypostasis after death. As a pathologic process, anemia may occur in consequence of thrombosis, embolism, pressure, arteriosclerosis, and other vascular changes.

Active hyperemia is characterized by diffuse redness of the mucosa. It usually depends upon infection with organisms which, like the gonococcus, enter from the urethra. The irritating influence of cantharides and other substances eliminated by the urine may also cause it.

Passive hyperemia usually depends upon obstruction of the inferior vena cava. It is characterized by catarrhal inflammation, dilatation, and varicosities of the veins of the bladder-walls. The dilated veins are especially numerous at the neck of the bladder, where they may obstruct its outlet, and when attenuated, may cause hemorrhages, either by spontaneous rupture or by injuries inflicted with introduced catheters, sounds, etc. The dilated veins frequently become the seat of thrombosis, and in them *phleboliths* commonly form.

Hemorrhage from the bladder may depend upon traumatic injury, calculus, malignant disease, tuberculosis, and the operation of certain parasites, especially the Bilharzia hæmatobium (*q. v.*).

Cystitis, or inflammation of the bladder, is a very common affection. In its acute form it is most frequent in gonorrhea; in its chronic form it results from calculus or enlarged prostate.

Acute cystitis is usually due to gonococci and other pyogenic cocci which gain entrance from the urethra, but may also be caused by poisons, such as cantharides, brought to the organ in the urine. It may result from unexpected trauma from the presence of previously latent calculi, or instruments used to explore the bladder. Infection of the urine in the bladder may also occasion it. Sometimes it occurs without discoverable cause.

The inflamed bladder is usually empty because of the frequent urination, which is one of the most characteristic symptoms. The contained urine is nearly always purulent or cloudy.

The mucous membrane is more or less injected, swollen, and edematous. In some cases pseudomembranous deposits may be found upon its surface. Such cases are most frequently seen in paralytic distention with attenuation of the walls.

The inflammation may extend from the mucous membrane *via* the lymphatic system to the submucosa and peri-urethral tissues, where suppuration occurs. The affection begins locally with the formation of swollen and hemorrhagic patches of necrotic superficial epithelium, upon which grayish pseudomembrane forms. Sometimes these patches become almost black in color, and are encrusted with phosphatic salts, especially when the urine is ammoniacal. When the entire lining of the bladder is affected, it appears much as if covered with a true diphtheritic membrane.

Phlegmonous cystitis consists of inflammation of the bladder, with infection of the surrounding cellular tissue and considerable suppuration. It usually depends upon rupture. The abscesses formed in the wall of the bladder appear upon its inner surface as soft yellowish projections which, when they rupture and evacuate, as often happens, leave ulcerations with undermined borders. Phlegmonous cystitis of this form is often described as *paracystitis phlegmonosa*.

Chronic cystitis may follow acute cystitis, but, as has been said, is more often due to enlargement of the prostate gland and the presence of calculi in the bladder, both of which conditions are associated with retention and decomposition of the urine, local congestion and irritation, hypertrophy of the muscular walls, and infection.

The mucous membrane of the chronically inflamed bladder is thickened, roughened, injected, reddened, sometimes polypose, not infrequently ulcerated, and may be covered with mucopurulent exudate. The finger-nail or the edge of a knife readily scrapes off layer after layer of epithelium.

The contained urine is usually alkaline, ammoniacal, purulent, and rich in mucus. Hemorrhages into the bladder-walls are frequent, and cause deep pigmentations of brownish or blackish color. Upon the denuded and ulcerated surfaces salts of the urates or phosphates readily collect. The muscular walls of the organ hypertrophy, the connective tissue increases in the submucosa, and the walls, when incised, seem to be thick and callous. The muscular hypertrophy is compensatory in order that the bladder shall be able to discharge its contents through the obstructed orifice.

A chronically inflamed and ulcerated bladder is always a source of danger from infection, which may rapidly terminate the patient's life.

Ulcer of the Bladder.—Ulcers of the bladder occur in both acute and chronic cystitis. An unusual form of cystic ulcer has, however, been pointed out by Rokitansky as *simple perforating ulcer of the urinary bladder.* It occurs in spinal palsy, and is characterized by a round necrosis of the wall of the organ, usually occurring upon the posterior inferior wall. It leads to rapid perforation, with the usual consequences.

Tuberculosis of the bladder is uncommon. Secondary tubercles are usually of hematogenous origin, though they may be lymphogenous when secondary to other forms of urogenital tuberculosis. The most frequent secondary tuberculous lesions occur in the form of small ulcers, usually situated in the inferior part of the organ, and extending into the submucosa.

The edges are infiltrated, and the surrounding mucous membrane injected. Secondary tuberculosis is much more frequent in men than in women, urogenital tuberculosis being more frequent in men. The affection usually begins in the epididymis, sometimes in the prostate, extends *via* the lymphatics to the vesiculæ seminalis, and thence to the bladder. In tuberculosis of the kidney or its pelvis, by which tubercle bacilli are discharged into the urine, the bladder resists direct implantation of the bacilli for a long time, and probably only becomes infected by bacilli distributed throughout its lymphatic vessels. The lymphatic circulation of the urogenital tract seems to be ascending, so that it is more frequent for tuberculosis of the testicle, prostate, seminal vesicles, and bladder to provoke simultaneous tuberculosis of both kidneys than for tuberculosis of the kidney to cause disease lower down.

The lesions consist of wide-spread ulceration, chiefly in the lower posterior portion of the viscus. The ulcerations present the usual appearances, having undermined infiltrated edges, cheesy, more or less excavated, centers, and partially detaching fragments of the mucosa, which project in a polypoid manner into the bladder. From the principal tuberculous ulcers, along the line of the lymphatic vessels, distributed miliary tubercles are found.

Secondary infection is readily possible, and precipitation of the urinary salts upon the ulcerated areas is common. The disease may destroy the greater part of the mucous membrane of the bladder.

Primary tuberculosis of the bladder is rare and of hematogenous origin. In its wall a single lesion with auxiliary outlying lesions may be found. The lesion may become as large as a walnut and be cheesy. The inner surface ulcerates, and the coagulation necrotic material from the center discharges into the bladder, forming a deep excavation.

Syphilis of the bladder is extremely rare.

Parasites of the Bladder.—**Echinococcus** cysts forming in the kidney or its pelvis occasionally rupture and discharge through the ureter into the bladder. In this way the hooklets may enter the urine. The eggs of Bilharzia hæmatobium and the embryos of filaria also occur in the urine from the same source.

The occurrence of echinococcus cysts in the bladder independently of primary disease of any other part is very rare.

Perforation of the intestine permits the occasional entrance of roundworms, pin-worms, and other objects from the intestine. The larvæ of flies have also been observed in the bladder, their eggs probably having been carried in upon a soiled catheter.

The trichomonas and cercomonas are also present in rare cases.

Bacteria of various kinds enter the bladder *via* the ureter, the urethra, from surrounding inflammatory lesions, through fistulas, and upon catheters. They produce decomposition of the urine and various inflammatory lesions.

Yeast plants often occur in diabetic urine, as do sarcina and oïdium.

Tumors of the Bladder.—Polypoid excrescences similar to those of other mucous membranes not infrequently develop upon the mucous membrane of chronically inflamed bladders.

Fibroma sometimes develops from the submucosa, and projects upon the inner surface of the bladder. It usually forms a small, pedunculated, villous mass, with long projecting processes, each consisting of a blood vessel surrounded by delicate areolar tissue and covered by stratified squamous epithelium. It is very frequently spoken of as *papillary tumor* of the bladder, and is one of the most frequent neoplasms of the organ. It does not invade the mucosa, but extends outward and may attain the size of a small apple. The tumor most frequently occupies the posterior inferior wall of the bladder, and may plug the urethra during micturition. It bleeds upon slight provocation, but is benign.

The epithelium covering the papilla is of an atypical columnar form. The hemorrhages from the tumor are frequent, and may be so severe as to cause the death of the patient from anemia. The papillary processes frequently break off, are passed with the urine, and enable one to make a microscopic diagnosis. Rarely the tumor closes the mouth of a ureter and produces hydronephrosis. The tumor may become incrusted with salts, and its processes becoming necrotic, break off. In this manner the tumor may be destroyed, removed, and replaced by an ulceration which, by subsequent cicatrization, permits spontaneous recovery. There is always danger that the tumor may, in the course of time, become malignant.

Myoma, fibromyoma, myxoma, sarcoma, fibrosarcoma, are of occasional occurrence.

Fibroadenoma of the bladder has been described. It occurs in the form of a tuber-like node, usually attached to the mucous membrane in the neighborhood of the trigonum and neck of the organ. It is seated in the mucosa, and may be sessile or pedunculated. It rarely becomes larger than a pigeon's egg, and in structure resembles the prostate gland, from which it probably originates.

Carcinoma of the bladder is usually primary, and is of the squamous epithelial variety—*squamous epithelioma*. It is not a common tumor, and its existence was at one time denied. It occurs, however, in both men and women as a nodular, spongy, papillary, fungous, or cauliflower mass, spreading over a considerable extent of bladder surface, and descending into the submucosa and muscularis. It is accompanied by numerous ulcerations, indurations, and round-cell infiltrations, and is a much less circumscribed, denser, and less elevated growth than the papilloma or papillary fibroma already described. Sometimes a large ulceration with indurated edges that reveal their true nature only upon microscopic examination results from rapid degeneration of such a tumor.

The vesical carcinoma readily extends to the rectum, and in women to the sexual organs. Primary carcinoma of the bladder is, however, a very rare affection of women. Metastasis rarely occurs in vesical carcinoma. The carcinoma rarely leads to perforation of the bladder, with its usual effects. It more frequently obstructs the ureters and causes hydronephrosis.

Secondary carcinoma of the bladder may occur from contiguity of tissue in cases of primary disease of the sexual organs, the rectum, and the prostate. Metastatic carcinoma of the bladder is extremely rare.

Cysts of the bladder may result from diverticula, the orifices of which become closed, and from patulous urachus. Of the parasitic forms, the echinococcus cysts may be mentioned, though they are very rare in occurrence. Paget has seen a case of *dermoid cyst* of the bladder.

Calculus.—Calculi are stones formed in the urinary organs in consequence of the precipitation of the salts of the urine. They are most common in the bladder. Early precipitation of the salts dissolved in the urine is a not infrequent phenomenon, and may be a cause of much suffering and many tissue alterations. The precipitated salts may occur in a molecular form, either amorphous or crystalline, and may collect in the kidney, descend to its pelvis, pass through the ureters, and collect in the bladder. The passage of the mineral substances in the urine in visible form is described as *gravel*, especially when made up of uric acid, which appears as a dark-red granular precipitate.

The urinary gravel is an indication of the existence of *lithemia* (*q. v.*), but by itself is of slight significance. It is when the salts precipitate in such manner as to form definite calculi or stones that they become locally important. It is convenient to speak of the various calculi according to the seat of occurrence.

I. **The Kidney.—Renal Calculus or Nephrolithiasis.**—The most frequent urinary deposits found in the kidney are uric acid and the urates. Various theories for the early precipitation of these substances have been propounded, but it seems most plausible that the condition depends upon errors of metabolism and oxygenation by which an excessive quantity of uric acid and the urates occurs in the urine. Cardiac and pulmonary diseases predispose to the condition. In fevers the errors of metabolism are most pronounced, while in all conditions in which the alkalinity of the urine is reduced the acid salts precipitate. Lead poisoning, lithemia, and gout are common causes. Fine crystals or amorphous granules of uric acid or sodium acid urate may be found in the uriniferous tubules, especially in the collecting tubes and in the connective tissue about the tubules. The discovery of the deposit may be made only with the microscope, and its extent limited to occasional collections of granules and crystals. At times there are considerable-sized accumulations which may obstruct the tubules. When the deposition is more marked, the knife, in incising the organ, grates upon the mineral deposits, and the eye and finger readily detect the presence of numerous scattered grains—*gravel*. The still more marked cases are characterized by the presence of *stones* or *calculi* which occupy cavities in the tissue—*retention cysts*. They are sometimes surrounded by encapsulating connective-tissue bundles of inflammatory new formation. The calculi vary from a pin-head to a walnut in size, the larger stones being found in the pelvis of the kidney rather than in its substance. The purely renal calculi are most frequent in the medullary substance.

The stones are irregular in shape, especially calculi that occur in the pelvis of the kidney and send prolongations into the calices. They have rough surfaces and are yellowish, reddish, or brownish in color. The stones are usually hard and brittle, sometimes crystalline, sometimes amorphous, in structure.

The *results of nephrolithiasis* will vary with its extent and degree. In the cases in which minute crystals or amorphous granules are found in the cells of the tubules and in the interstitial tissue of the kidney no structural changes occur. When cellular degenerations exist, it is always more or less of a question whether they may have caused the mineralization or resulted from it. Larger formations damage the contiguous tissue, bring about atrophy, and subsequently occupy spaces bounded by more or less well-developed connective-tissue walls.

Nephrolithiasis, whether the stones be situated in the kidney or in its pelvis, predisposes to suppuration, the infection probably occurring through the ureter from the bladder, thus bringing about abscess of the kidney (*q. v.*).

II. **The Ureter.**—Calculi found in the ureter are probably rarely formed there, but descend from the pelvis of the kidney when the ureter is unusually dilated, and then lodge as it contracts. They may cause obstruction with local inflammatory, ulcerative, and phlegmonous changes. Secondary changes, such as hydronephrosis, may occur if the stones cannot pass on into the bladder. The passage of calculi through the ureters is accompanied by intense pain (renal colic).

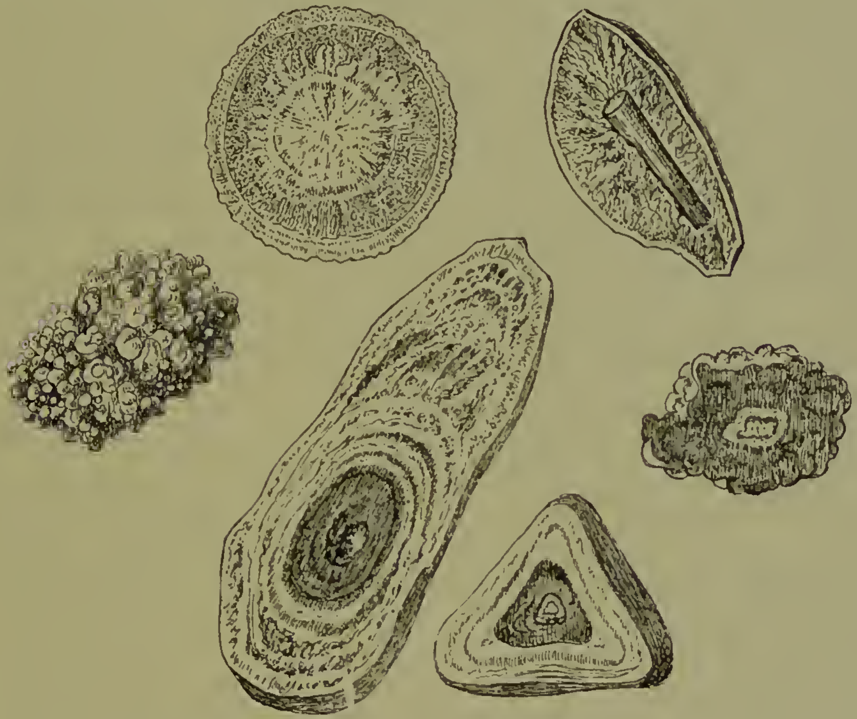

FIG. 350.—Urinary calculi showing the nuclei from which they originate, the concentric lamina by which they are formed, the radiating infiltration sometimes observed, and the various smooth and nodular surfaces (Orth).

III. **The Bladder.**—**Vesical** or **cystic calculi** are most common, and, therefore, most important to the clinician. They are composed of substances either normal to the urine or derived from it, precipitated uric acid and urates being the most frequent. The greater the time the urine is retained in the bladder, the more excellent are the opportunities for precipitation of the salts and increase in the size of the calculi. The outlet is, however, large enough to permit the escape of masses that would merit considerable attention higher up, and the passage of *gravel* with the urine is common.

How many of the cystic calculi originate in the bladder cannot be determined. The fact that the passage of formed calculi from the pelvis of the kidney to the bladder is of frequent occurrence, together with the knowledge that calculi form readily about foreign bodies in the bladder, suggests that many vesical calculi owe their beginning to stones descending from the kidney. On the other hand, there is no doubt but that vesical calculi can occur without previous nephrolithiasis, as is shown by stones formed of salts rarely precipitated in the kidney, and by calculi having nuclei that did not originate in the kidney—foreign bodies, etc.

The causes predisposing to cystic calculus vary with the nature of the calculus. Thus, while the uric-acid calculus probably occurs most frequently in lithemic conditions, and the phosphatic calculus in phosphaturia with ammoniacal decomposition of the urine, there are many cases in which the drinking of alkaline waters—lime-waters—can be put down as the chief predisposing factor.

The cystic calculi are usually single, rounded or ovoid in form, and vary in color and consistence with their composition. When multiple, they may be faceted like gall-stones.

Uric-acid Calculus.—This consists either of pure uric acid or of the urates.

(*a*) The pure uric-acid calculus is usually rather small—the size of a pea or a pigeon's egg, of a yellowish, reddish, or brownish color, rough and crystalline on the surface, and brittle. These stones probably originate in the pelvis of the kidney.

(*b*) The urate calculus may contain uric acid, urate of ammonium, urate of magnesium, oxalate of calcium and ammoniomagnesium phosphate, in addition to the chief ingredient, uric acid. These stones are larger than the pure uric-acid calculus, and commonly attain the size of a hen's egg. Their structure is laminated, as they often form about a central nucleus. The outer or rind layer often contains the oxalate of calcium. The surface is likely to be smooth; the stone is pale in color.

Stones consisting of urate of ammonium are usually small—not larger than a pigeon's egg, rounded, and somewhat flattened. Their color is dull yellow, the surface finely granular, the texture friable, the fractured surface granular. Stones of urate of magnesium have an ashen-gray color.

Phosphatic Calculi.—These are of common occurrence and consist of: (*a*) Phosphate of calcium; (*b*) ammoniomagnesium phosphate, and (*c*) calcium carbonate.

The stones are white or gray in color, and may be hard and brittle, though more likely to be soft and crumbling. They may attain considerable size. The most frequent ingredient is probably the ammoniomagnesium phosphate, and the stones which contain most of this salt are the softest. The carbonate of lime calculi are rare, pure white in color, and chalky.

It is not infrequent for a stone to be composed of all of these ingredients.

The formation of phosphatic calculi is distinctly favored by stricture of the urethra, enlargement of the prostate, and other conditions by which the urine is retained in the bladder and predisposed to ammoniacal fermentation. The stones not infrequently form about foreign bodies and small calculi of uric acid or urates.

Oxalate Calculi.—These are less frequent in occurrence. They are characterized by a brownish color and a peculiar surface, which is spinous or coral-like, and full of irregular projections of a rounded, spinous, or club-like form. Their substance is very hard. The stones are commonly mixed in composition, uric acid being an important ingredient.

Cystin Calculi.—These are uncommon. They are soft and waxy in consistence, brownish or sometimes greenish in color, and are usually small in size and ovoid in form. The fractured surface is crystalline. Cystin stones have been observed in the pelvis of the kidney.

Xanthin Calculi.—These are extremely rare calculi of small size and brownish or cinnabar-red color. The surface is usually smooth. The consistence is brittle, and the surface of fracture amorphous.

In rare cases calculi may be formed of silicic acid, benzoic acid, sulphate of calcium, and indigo. One of the latter, described by Ord, weighed 40 grams and was found in the kidney.

Gall-stones sometimes enter the bladder by fistula formation, and then become transformed to cystic calculi by subsequent precipitation of uratic salts.

In vesical calculus the mucous membrane is in a state of chronic inflammation, with erosion and ulceration of the surface and occasional mineralization of the eroded areas. The inflamed condition and presence of the foreign body stimulate the organ to frequent and violent contractions, which with difficulty discharge the urine through the urethra obstructed at its orifice by the calculus. The result is hypertrophy of the muscular coat. Hyperplasia of the connective tissue of the submucous coat also occurs, and diverticula frequently form. Hydronephrosis may result from the obstruction.

DISEASES OF THE URETHRA.

Urethritis, or **inflammation of the urethra,** is the most frequent and most important lesion.

Etiology.—It is nearly always infectious, and in the great majority of cases depends upon the gonococcus of Neisser. It is sometimes caused by Staphylococcus pyogenes, more rarely by the streptococcus, and still more rarely by the colon bacillus and other micro-organisms. The disease is occasionally of traumatic origin, being caused by the introduction of dirty sounds and foreign bodies into the urethra.

The most frequent form of urethritis is catarrhal. It is characterized by the formation of pus, desquamation of epithelium, occasional follicular abscesses, and, if gonorrheal, by a tendency to invade the tissue farther and farther back until it not infrequently reaches the bladder. The pus has a creamy character, though it is sometimes greenish yellow. As the inflammation subsides it becomes thinner and mixed with mucus (*gleet*).

Except by the history of infection and the presence of gonococci in the pus and epithelial cells in the exudate the gonorrheal urethritis has no essential differences by which it can be separated from other forms. Indeed, in gonorrhea the infection is commonly mixed, and staphylococci occurring together with the gonococci are responsible for many of the complications. The inflammation usually heals readily without marked anatomic alterations. It may, however, be complicated by folliculitis, vesiculitis, cystitis, orchitis, prostatitis, vaginitis, etc. One of the most frequent complications is cicatricial formations in the floor of the urethra, by which a stenosis or *stricture* occurs. Such *strictures* are frequent in men, but almost unknown in women, and usually occur in chronic urethritis or *gleet*. They may follow traumatic simple or gonorrheal urethritis. The strictures may consist of simple swelling of the mucosa, cicatricial bands, peri-urethral connective-tissue formations, the stenosis extending along the canal for some distance. They are most frequent in the membranous part of the urethra, next most frequent in the spongy portion, near the membranous urethra. Stenosis of the urethra, from hypertrophy of the prostate gland, also occurs in old men.

Croupous and **diphtheritic urethritis** are rarely observed.

Syphilitic and **tuberculous** inflammations, with the usual indurations, tubercles, ulcers, and infiltrations, are rare. *Chancroid* sometimes occurs in the urethra near the meatus urinarius.

Polypoid excrescences may form and show a structure similar to the papilloma; they appear as small, tumor-like projections. Obstruction of the glands in and at the meatus urinarius, especially in women, may cause the formation of small retention cysts.

Traumatic injuries, ulcerative diseases, and peri-urethral abscesses sometimes lead to the formation of fistulous communications with the exterior. Through such fistula the urine escapes during micturition.

Tumors of the Urethra.—These much more frequently arise from the neighboring structures, and invade the urethra by continuity of tissue, than from the urethra itself. In men, *epithelioma* of the glans penis commonly invades the urethra near the meatus, and *carcinoma* of the prostate encroaches upon the urethral canal and sometimes obstructs it. In women, *sarcoma*, *myxoma*, *fibroma*, and *carcinoma* have been observed. A small tumor, usually a cavernous fibroma known as a *caruncle*, is often found at the meatus in women.

Parasites rarely occur in the urethra. The pin- or thread-worms sometimes enter the meatus during their migrations. I have, however, observed a case of myiasis of the urethral and peri-urethral tissues in a man, a paralytic, who had not been properly protected from flies, and who was kept in a filthy condition.

Calculi occasionally form in the urethra. When present, they usually occupy the *fossa navicularis*. They have been known to attain the size of a date-stone and obstruct the outflow of urine. It is probable that the stones are not originally formed in the urethra, but descend from the bladder, and, failing to escape through a contracted meatus, remain and increase in size by subsequent incrustation.

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